UNIVERSITY OF STRATHCLYDE

DEPARTMENT OF BIOMEDICAL ENGINEERING

ASSESSMENT OF FETOSCOPIC TRACHEAL OCCLUSION USING ULTRASOUND IMAGES IN PHANTOM STUDY

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DECLARATION OF AUTHENTICITY

This thesis is the result of the author's original research. It has been composed by the author and has not been previously submitted for examination which has led to the award of a degree.

Signed: Date:

ABSTRACT

Congenital Diaphragmatic Hernia (CDH) is a birth defect that affects approximately 1 in 2000-5000 neonates. Most of the CDH cases are isolated, which means that affected individuals have no other major malformations. The diaphragm is a muscle that separates the chest from the abdomen. Incomplete fetal diaphragm formation results in a hernia that allows the abdominal organs to move into the chest and crowd the heart and lungs. This crowding can lead to pulmonary hypoplasia. Newborns with underdeveloped lungs have severe respiratory insufficiency.

The outcome of fetuses with CDH may be improved by fetal endoscopic tracheal occlusion (FETO). During pregnancy, fetal lungs secrete fluid into the amniotic cavity through the airways. FETO is a minimally invasive therapy which objective is to stimulate pulmonary growth. Through a small incision in the skin a very small fetoscope is inserted and advanced through the mouth of the fetus down to the trachea, where a detachable balloon is inflated. The fetus is left with the balloon inside the trachea with a completely obstructed airway and after 3-6 weeks it is removed by endoscopy. The obstruction of the trachea prevents the egress of pulmonary fluid triggering lung expansion and growth and decreasing pulmonary hypoplasia. Even though FETO saves many babies' life, the procedure has some drawbacks. Surgeons make use of rigid fetoscopes to introduce the balloon into the trachea. Fetuses are forced to be in a hyperextended neck position during the surgery so that the access to the trachea is possible. There are many concerns about the cervical vertebrae stress and fetal distress that the hyperextension could cause to the fetus. The fetal neck positions throughtout the surgery were assessed and measured by means of ultrasound images. The results show that the babies undergo a neck hyperextension of great magnitude that undoubtedly might lead to fetal damage and distress.

ACKNOWLEDGEMENTS

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LIST OF ABBREVIATIONS

CDH	Congenital Diaphragmatic Hernia
FETO	Fetoscopic Endotracheal Occlusion
ECMO	Extracorporeal Membrane Oxygenation
ICR	Instantaneous centre of rotation
LHR	Lung-to-head ratio
PPROM	Preterm premature rupture of membranes
BPD	Biparietal diameter
OPD	Occipitofrontal diameter
HC	Head circumference
LT	Length of the trachea
CSA	Cross sectional area
LBT	Length of bronchial trees
D	Diameter of the trachea
LH	Larynx height
PH	Pharynx height
TGC	Time gain compensation
ICR	Instantaneous centre of rotation

1 INTRODUCTION

Some congenital prenatally detected anatomies can be treated after birth. However, in some cases prenatal surgery would save fetuses' life or prevent permanent organ damage. Fetal surgery for congenital diseases has become vital for those fetuses who would not survive gestation or would experience significant morbidity and mortality after birth[1-3]. The outcome of fetuses with congenital diseases improves considerably after surgery. Imaging technologies such as Ultrasound and MRI, and amniotic fluid testing are methods of diagnosis of congenital malformations. The possibility of diagnostic congenital anomalies before birth is what opened the door to fetal surgery. Until diagnostic technologies were not available fetal surgery could not been performed. The introduction of ultrasonic diagnosis of fetal congenital malformations in the 1970s made possible the correction of congenital diseases in-utero[3]. During several years trials and experiments of fetal surgery were done in animals. In 1981 the first open fetal surgery was performed in humans[4]. Open surgery implies the opening of the uterus, allowing surgeons to work directly on the fetus. The uterine incisions that are required for fetus exposure, are an important source of complications. The premature rupture of membranes is the most common side effect of open fetal surgery, which sometimes results in preterm labor[5]. During the last three decades, significant advances in surgical techniques and diagnosis technology has made possible the evolvement of fetal surgery to a minimally invasive procedure. In the 90s, due to the popularity of the video-endoscopic surgery and the earlier experience with fetoscopy, the concept of endoscopic fetal surgery appeared[6-8].

Congenital Diaphragmatic Hernia, CDH, is one of the congenital anomalies that require fetal surgery. When fetal diaphragm fails to develop completely, there is an opening on it called hernia. The problem arises when abdominal organs pass through the hernia and move into the chest compressing the heart and the lungs. The lungs do not have enough space to grow completely, leading to pulmonary hypoplasia and pulmonary hypertension. When babies with this condition are born, they have life-

threatening respiratory difficulties due to the pulmonary hypoplasia[9-11]. Even though surgeons repair the diaphragmatic hernia, most of them do not survive after surgery because their lungs are not enough developed. Currently, the surgical procedure used to improve lung growth and give those babies a better outcome is Fetoscopic Endotracheal Balloon Occlusion (FETO). A fetoscopic sheath equipped with a fetoscope and a balloon occlusion system is used to insert an inflatable detachable balloon into the fetal trachea, blocking the airways. This blockage will lead to lung growth[12,13].

In fetal surgery, surgeons use rigid fetoscopic sheaths to guide and protect the scope during the surgical procedure. The neck of the fetus has to be in a position that makes possible the insertion of the fetoscope into the trachea, where the balloon is inflated and detached. Using rigid equipment requires the manipulation of the fetus before surgery, causing cervical vertebrae stress and fetal distress[14]. Moreover, during the surgical procedure the surgeons use the fetoscope to force the neck hyperextension so that the fetoscope can be advanced down into the trachea. The forces and pressures may cause injuries in some delicate tissues and structures of the fetus.

LITERATURE REVIEW

2 RESPIRATORY SYSTEM

2.1 RESPIRATORY SYSTEM

The human respiratory system is made up of tissues, blood vessels and organs that work together so that we can breathe. The fundamental function of the respiratory system is to provide every part of the body with rich-oxygen blood. When we breathe, we inhalate rich-oxygen air and we exhalate air containing CO_2. By doing this we fill the lungs with oxygenated air so that the blood can be oxygenated and we get rid of waste gas.

The respiratory system can be subdivided into two sections. The upper respiratory tract which consists of nose, pharynx and larynx and the lower respiratory tract which includes the trachea, the bronchial tree and the lungs[15,16].

The air enters the respiratory tract through the external nares or through the mouth. Most of the respiratory system is covered by mucous membranes, which secrete mucus. This substance filters and cleans the air, preventing the passing of dust, bacteria and other harmful products to the lungs. After being filtered, the air passes to the pharynx and then into a second chamber called larynx. When food is ingested it passes though the pharynx before entering into the esophagus. The epiglottis, which is a tissue that covers the entrance of the larynx, prevents the food to enter the larynx deviating it to the esophagus. Once in the larynx the air passes into the trachea, which divides into left and right bronchial trees. The bronchi branch into smaller airways called bronchioles. Each bronchiole is surrounded by air sacs called alveoli. The gas exchange takes place across the thin walls of the alveoli. Breathing is a continuous cycle. Oxygenated blood is pumped by the heart to the rest of the body, proving tissues and organs with oxygen. In that moment the blood is losing oxygen

and it becomes deoxygenated blood which goes back to the heart and is sent to the lungs where it is oxygenated again [15,16].

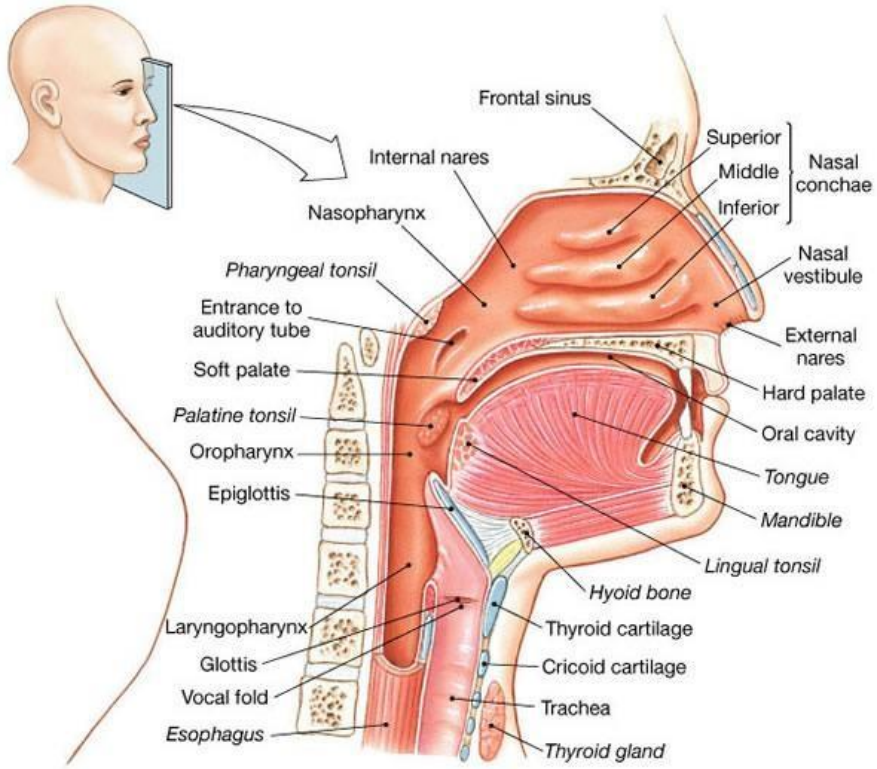

Figure 1. Upper respiratory system anatomy [1]

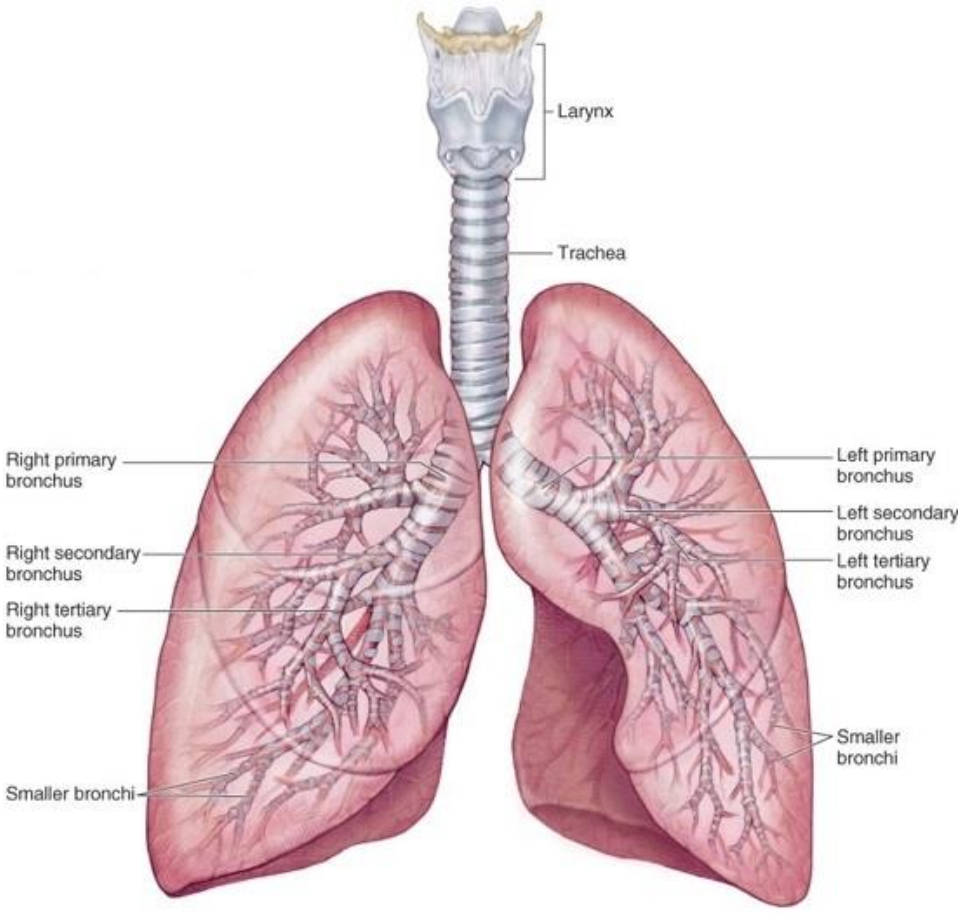

Figure 2. Lower respiratory system anatomy **[2]**

2.1.1 Trachea

The trachea is a flexible air-conducting tube 10 to 12 cm long and with a diameter that varies from 2 to 2.5 cm. Through it, we introduce air in our lungs. It is made up of imperfect ring of hyaline cartilage, fibrous tissue, muscular fibers, mucous membrane and glands. It starts at the lower part of the larynx, at the sixth cervical vertebra. Approximately at the level on the fourth or fifth thoracic vertebra it bifurcates into the left and right bronchial trees. The right bronchi is wider, shorter and more vertical that the left one[16, 17].

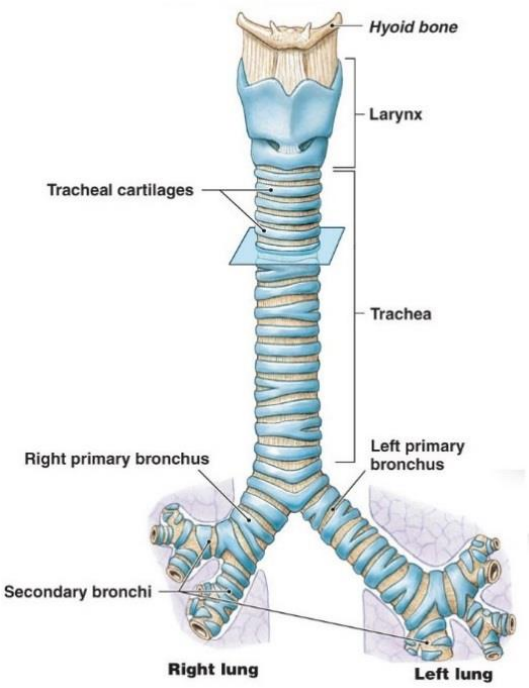

Figure 3. Trachea and bronchi **[3]**

As mentioned before, the gas exchange takes place into the lungs, concretely in the alveoli. In case the lungs cannot accomplish their function the blood is not oxygenated leading to hypoxia and the body cells die. Therefore, the lungs are a vital organ and it is extremely important to keep them in a healthy state at all times.

They take up most of the space in the thoracic cavity and they are surrounded by the pleura, which is a thin double-layered membrane whose main purpose is to protect the lungs from harmful substances or surrounding areas of the body that might harm them[15-16,19].

2.1.2 Development of the respiratory system

In human fetuses the structural and vascular development of the lungs starts at the 3rd week of gestation as primitive lung buds and it finishes postnatally. The number of alveoli at birth is approximately 20-50 million[24]. Alveoli are generated until the baby is 2-3 years old and its surface area increases until the adolescence[30]. Fetal lung fluid secretion and fetal breathing movements are two key parameters for fetal lung growth[25]. Amniotic fluid volume also contributes to the fetal lung distension and hence lung growth[20-23]. Fetus who are born prematurely or whose lungs could not grow completely before birth will experience life-threatening respiratory difficulties right after birth.

Lung development is divided into five stages: embryonic, pseudoglandular, canalicular, saccular and alveolar period[23,26].

STAGE	TIME	PROCESSES
Embryonic	3-7 weeks	Formation of: ▪ Trachea ▪ Bronchial trees and segmental bronchi ▪ Vasculogenesis of airway buds
Pseudoglandular	7-17 weeks	Formation of: ▪ Terminal bronchioles ▪ Major blood vessels of the lung
Canalicular	17-27 weeks	Formation of: ▪ Respiratory bronchioles ▪ Alveolar ducts And further lung vascularization
Saccular	28-36 weeks	Formation of: ▪ More alveolar ducts ▪ Surfactant
Alveolar	36 weeks to 2-3 years	Formation of: ▪ Alveolar sacs ▪ Surfactant

Table 1. Lung development stages

2.1.3 Amniotic fluid and its function in lung development

Pregnant women have an amniotic sac inside of the uterus. This sac contains the growing fetus and amniotic fluid. The amniotic fluid keeps the fetus warm, preventing heat loose, and it acts as a shock absorber, the baby is protected from shocks coming from the outside. The developing baby is floating in the amniotic fluid, moving in the womb what helps to strengthen his muscles and his bones[28].

The amniotic fluid is composed by 98% of water and 2% of salts and cells from the fetus[29]. During the first four months of gestation the amniotic fluid is produced by the mother's body until the fetal kidneys start working. For the rest of the gestation the fetus swallows amniotic fluid, it goes through the digestive and urinary system and is released into the amniotic fluid again. This process helps the fetus to develop, practice and streghthen the urinary and digestive system before birth.

The balance between fetal fluid production and resorption keeps the right amount of amniotic fluid surrounding the fetus. Either an excessive amount of amniotic fluid (polyhydramnios) and an abnomally small amount of amniotic fluid (olygohydramnios) are a sign of swallowing reflex fetal problems, this may be due to fetal abnormalities or congenital anomalies among others[30,33].

During pregnancy the fetal lungs are filled with a fluid made up mostly of water that is produced by the lungs continuously. The liquid accumulates in the airways because the vocal cords located at the top of the trachea prevent its egress. This fluid accumulation makes the lung pressure to increase and the airways are stretched resulting in lung growth[12,13]. The fetus secretes lung fluid into the amniotic sac through fetal breathing movements. The vocal cords open and the fluid escapes from the lungs due to the higher pressure in the lungs. This cyclic changes of pressure and the stretching of the airways produces lung development before birth[34]. Once the baby is born vaginally, the passage through the vaginal opening compresses the baby's thorax and the liquid is released. If the baby is born via C-section the squeezing does not occur and it is more likely that respiratory complications appear.

2.1.4 Diaphragm

The diaphragm is a muscle that performs two very important functions in human body. It physically separates the abdominal and the thoracic cavity and it is the primary muscle of respiration. The diaphragm has three opening that allow the passage of the inferior vena cava, the aorta and the esophagus[15-16].

The diaphragmatic development involves multiple layers of tissue. It is in the 4th week of gestation when it begins to form, with the appearance of the peritoneal fold, which form from the lateral mesenchymal tissue. At the same time, the septum transversum is formed from the inferior portion of the pericardial cavity. The septum transversum provides an incomplete separation between the thoracic cavity and the abdominal cavity. On either side there are two pericardioperiotoneal canals, which

are closed off later on by the pleuroperitoneal membranes. The complete closure of the canals is achieved at the 8th week of gestation[35-36]. If one of the canals fails to close, a diaphragmatic congenital hernia appears[37]. The existence of that opening in the diaphragm would allow the passage of abdominal organs to the chest. In that case, the lungs would not have enough space to develop and grow completely and the fetus would present pulmonary hypoplasia[37].

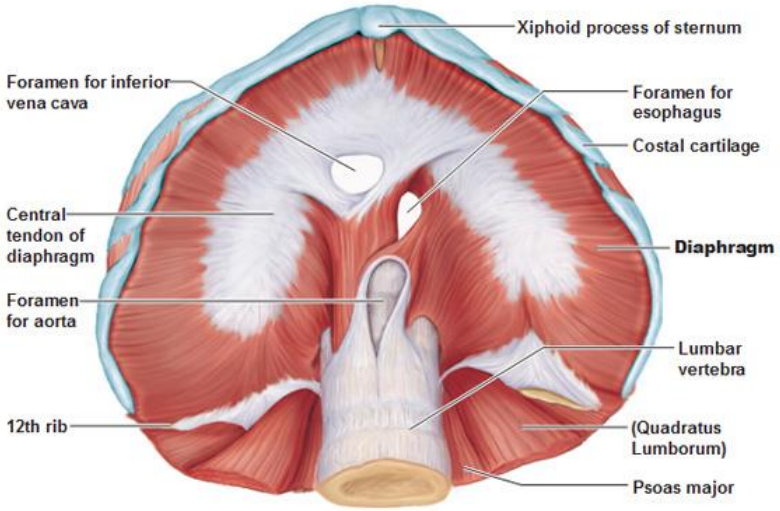

Figure 4. Diaphragm anatomy **[4]**

2.1.5 Respiratory mechanisms

Human beings need to breathe in order to introduce O_2 into the lungs and get rid of CO_2 so that the blood can be oxygenated in the lungs, by means of gas exchange in the alveoli. The breathing, also called external respiration, is divided into two stages, inhalation and exhalation. During inhalation the intercostal muscles and the diaphragm contract expanding the thoracic cavity. The pressure in the lungs decreases and air is introduced in the lungs. This air is rich in O_2. When exhalation takes places, the diaphragm and the intercostal muscles relax and return to its usual position. The chest cavity reduces in size and the lung pressure increases and so air with a high concentration of CO_2 is forced out of the lungs[16,38].

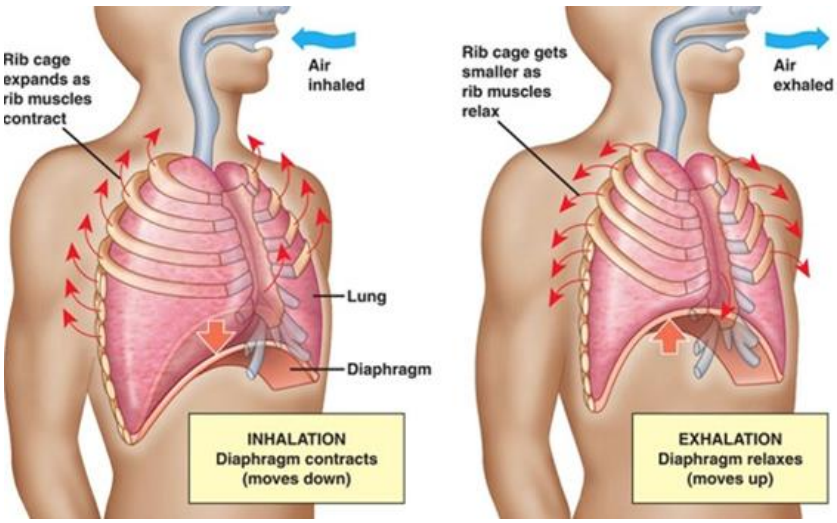

Figure 5. Breathing mechanism **[5]**

3 PRENATAL AND POSTNATAL CIRCULATION

As mentioned before, fetal lungs are filled with amniotic fluid and gas exchange does not take places in the lungs but in the placenta[39]. Oxygen and nutrient rich blood leaves the placenta and goes to the liver via the umbilical vein. Most of this blood bypasses the hepatic circulation passing through the ductus venosus[39,40]. In the ductus venosus the blood is mixed with deoxygenated blood that comes from the portal vein and passes to the inferior vena cava (IVC). In the IVC the blood is mixed with more deoxygenated blood that returns from the legs and the thunk and is carried to the right atrium. Once in the right atrium the blood is shunted through the foramen ovale to the left atrium, bypassing non-functional lungs[39,40]. From the left atrium the blood flows to the left ventricle through the mitral valve and then is pumped into the aorta which carries it to the rest of the body. The right atrium also receives blood from the superior vena cava (SVC), this blood is poor oxygen blood that returns from the head and arms. Most of this blood passes flows into the right ventricle by the tricuspid valve and is pumped out to the pulmonary trunk. By means of the ductus arterious, most of the blood that is passing through the pulmonary trunk goes to the descending aorta which carries semi-oxygenated blood to the legs and to the gut[39.40]. The descending aorta has a branch that go to the umbilical arteries, which carry deoxygenated blood and metabolic waste to the placenta where gas exchange occurs.

At birth the circulatory system experiences a radical change. Once the baby is born, the umbilical cord is clamped, the exchange of blood with the placenta ends and the ductus venosus that connects the umbilical vein with the IVC is occluded. In that moment is when breathing through the lungs starts. During inhalation the lungs are expanded, the pulmonary vessels dilate and the pressure in the pulmonary system decreases[40]. Due to this pressure decrease the blood is not shunted anymore through the ductus arteriosus and it closes normally within the 15 to 18 hours after birth[41]. The pressure in the left atrium increases due to the blood that is flowing back from the lungs and the pressure in the right atrium falls. This pressure difference produces

the closure of the foramen ovale[41]. Once all the shunts are closed the postnatal heart blood circulacion starts.

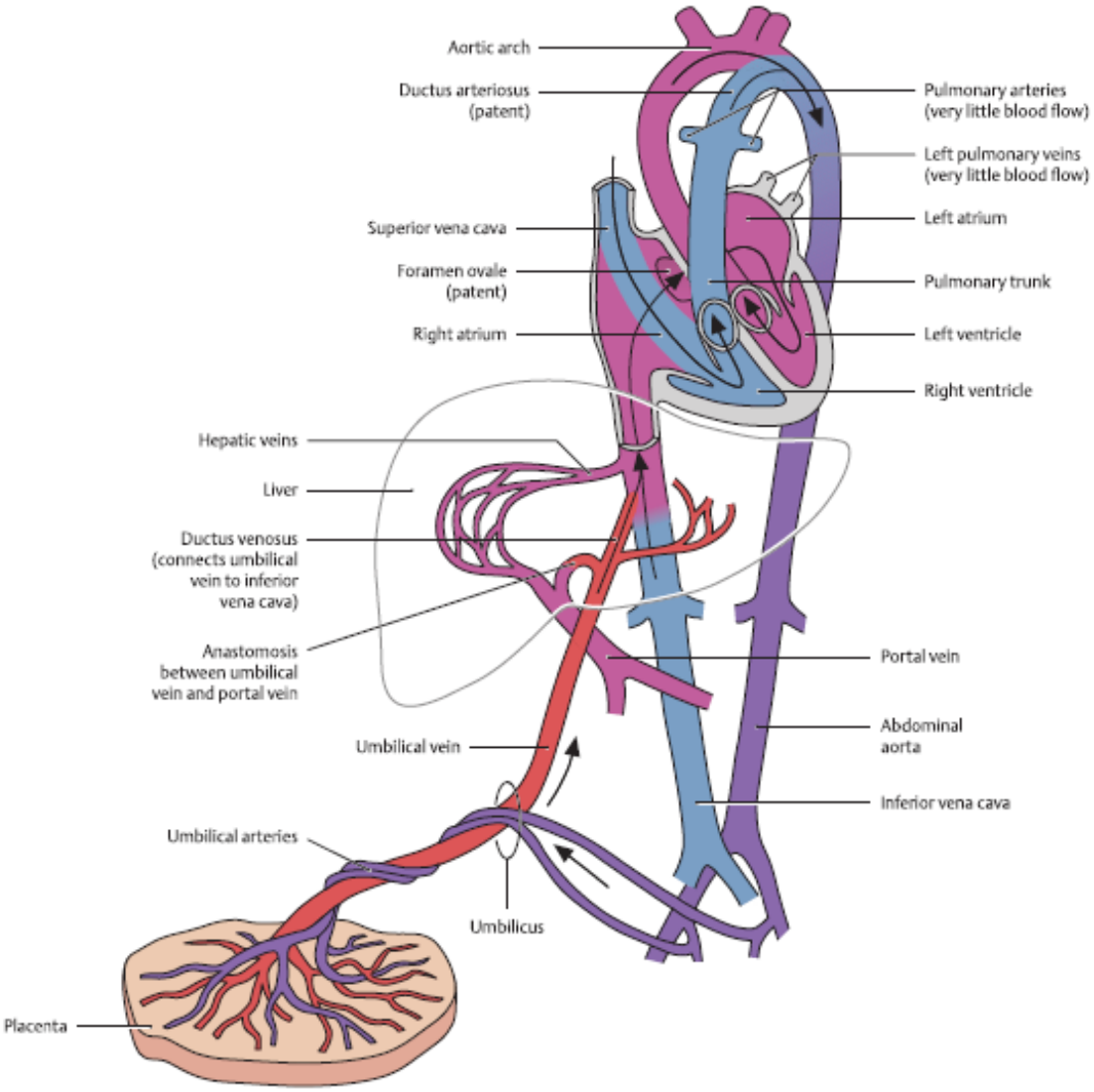

Figure 6. Prenatal circulation **[6]**

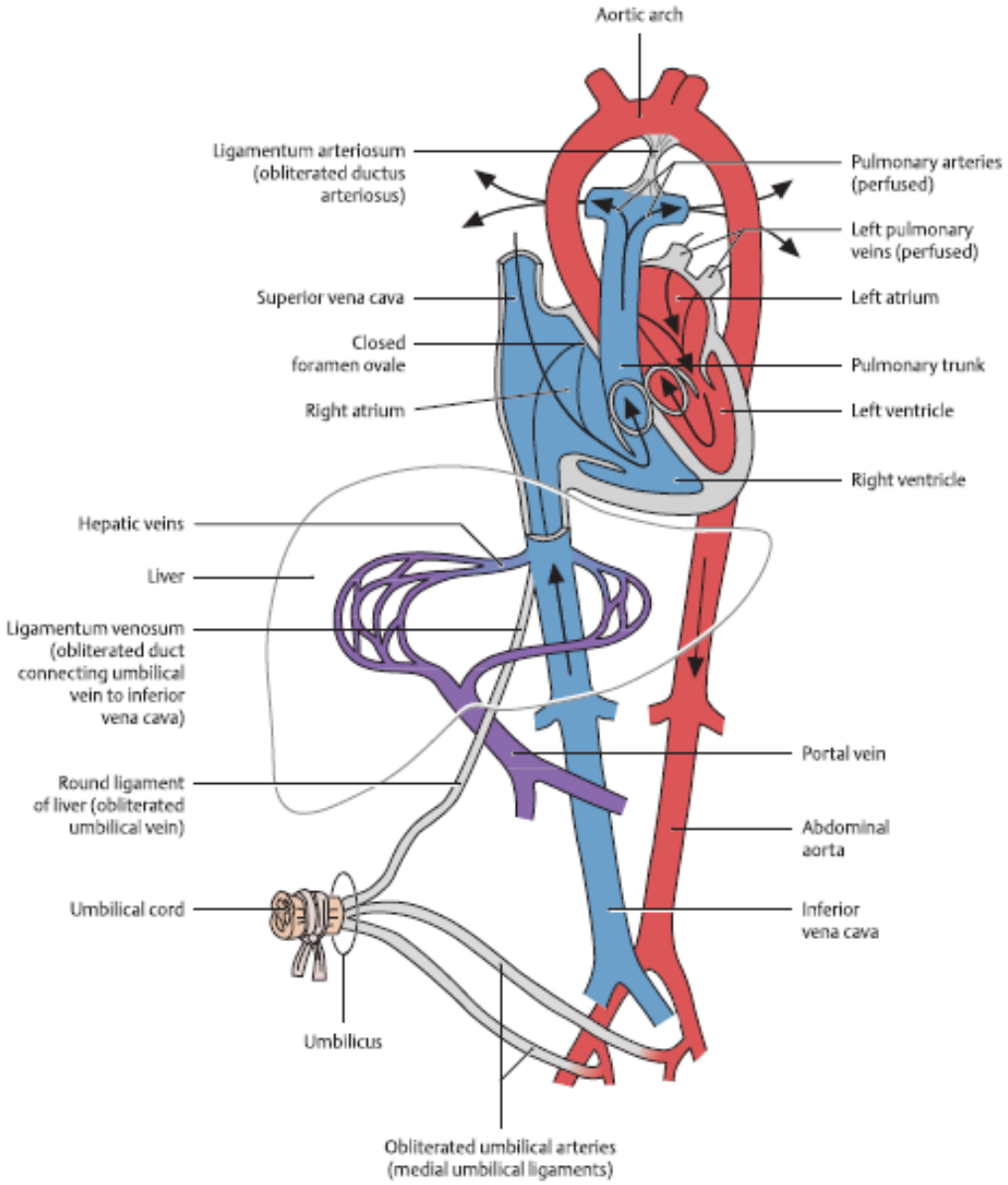

Figure 7. Postnatal circulation **[6]**

4 ANATOMY OF THE SPINAL COLUMN

The vertebral column, also known as spinal column, is the central axis of the body. It protects the spinal cord and the spinal nerves. It carries the weight of the upper part of the body and it provides movement to the neck and back. It is made up of 33 vertebrae and can be divided into five different regions: cervical, thoracic, lumbar, sacral and coccygeal region.

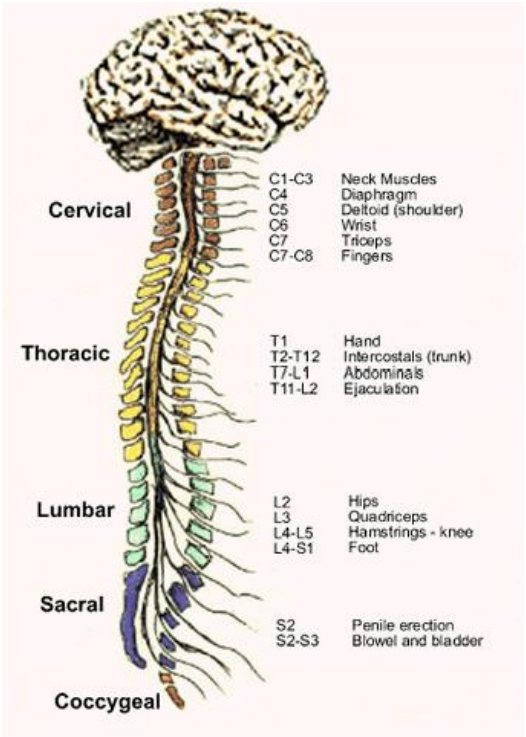

Figure 8. Regions of the column vertebrae **[7]**

The intervertebral discs are soft tissue structures situated between each vertebra. They act as shock absorbers. Each disc is composed by a central core of gelatinous and highly hydrated material, known as the nucleus pulposus (NP), a surrounding series of concentric rings of fibrous cartilage, known as annulus fibrosis (AF) and the end plates[42].

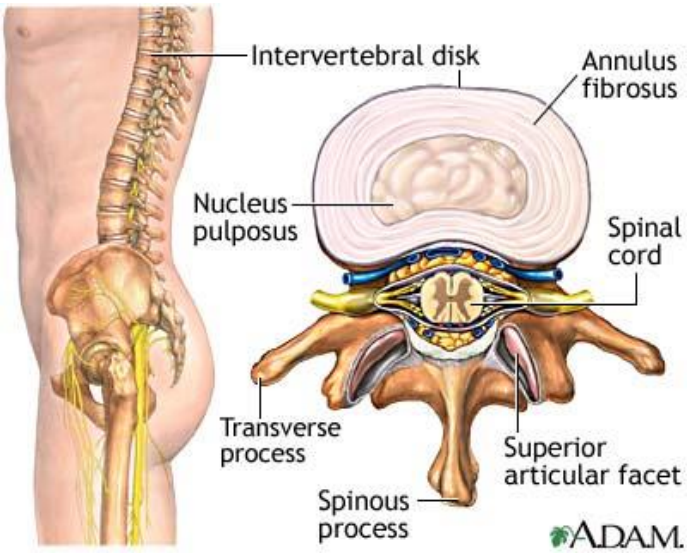

Figure 9. Intervertebral disk **[8]**

The region of the spinal column that I focused my research on, it is the cervical region. It is the part of the column vertebrae that lies along the neck in front of the spinal cord and it consists of seven vertebrae. It starts in the base of the skull and extends down to the thoracic spine. Its main function is to support the neck and the head.

During flexion and extension each cervical vertebra rotates around an instantaneous centre of rotation (ICR) which changes at every instant of time. The ICR is situated in a very small are somewhere within the spinal vertebra.

The instantaneous axis of rotation (IAR) is an axis about which a vertebral rotates at some instant of time. For normal spinal units, the IAR for each of the rotary modes (flexion, extension, lateral bending, and axial torsion) is confined to a relatively small area somewhere within the vertebral unit.

Penning found that the position of the ICRs is different in every cervical vertebrae. At lower cervical levels, the ICR is located close to the intervertebral disk but, in vertebrae situated at higher cervical levels the ICR is located closer to the centre of the segment[43].

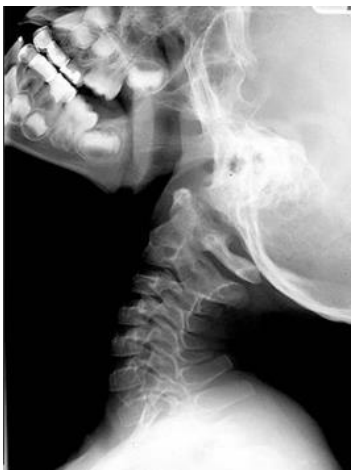

Figure 10. X-ray image showing extension of the cervical vertebrae **[9]**

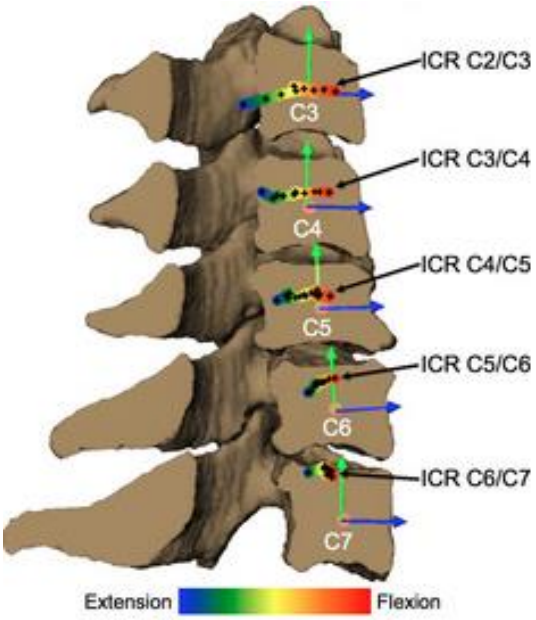

Figure 11. Position of ICR for cervical vertebrae flexion and extension **[10]**

5 CONGENITAL DIAPHRAGMATIC HERNIA

Congenital Diaphragmatic Hernia (CDH) occurs when the diaphragm fails to form completely. One of the causes of this malformation is failure in the closure of the pericardioperioneal canals[37]. This congenital defects allow the herniation of the abdominal organs into the chest limiting the space for the lungs to grow completely, leading to varying degrees of pulmonary hypoplasia and pulmonary hypertension[45, 46]. At birth, the lungs will not be big and strong enough to make the gas-exchange. There will be high blood pressure within the pulmonary vessels because are fewer in number are stiffer.

The etiology of CDH is still unknown. It is a sporadic congenital defect that affects to 1 in 2000 to 5000 live births. Most of the affected fetuses do not present any other abnormality, in this case it is called Isolated Congenial Diaphragmatic Hernia [10, 12].

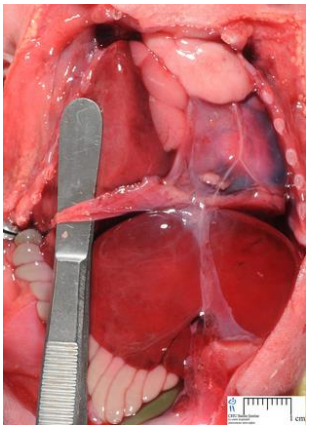

Figure 12. Fetus with congenital diaphragmatic hernia **[11]**

5.1 TYPES OF CDH

The most common diaphragmatic hernia is the Borchdalek hernia, is a postlateral defect that occurs when the pleuroperitoneal membranes fail to close. This defect can appear either on the left or on the right side of the diaphragm[47,48]. The 80% of

these defects are left-sided, probably because the right pericardioperitoneal canals close before the left ones[49]. When the herniation occurs in the left side the thorax may contain the small and large bowel, the spleen, the stomach, the left lobe of the liver and occasionally the kidney. When the defect appears in the right side of the diaphragm, the right lobe of the liver and sometimes the bowel and the kidney may herniate into the chest[50].

The Morgagni hernia is usually a very small hernia that occurs in the 1-2% of the cases. It is a parasternal defect located in the anterior portion of the diaphragm. It is the result of the incomplete fusion of the septum transversum and the sternum with the anterior ribs[51].

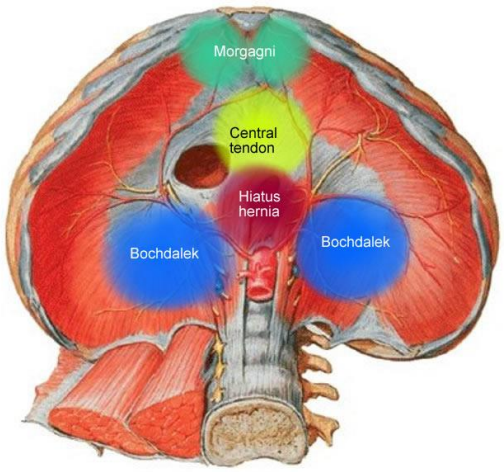

Figure 13. Types of diaphragmatic defects **[12]**

5.2 CONSEQUENCES OF LUNG UNDERDEVELOPMENT

Congenital diaphragmatic hernias appears at 8-10 weeks gestation. The bronchial tree is fully developed in the 17th week of gestation so the herniated abdominal organs would affect lung growth and maturation, resulting in pulmonary hypoplasia and pulmonary hypertension. The hypoplastic lungs not only are smaller but have fewer alveoli, diminished alveolar air space and alveolar gas-exchange surface area.

Apart from that, the pulmonary vasculature of hypoplastic lungs has an abnormal growth, presenting a decrease in total size of the pulmonary vascular bed, fewer vessels per unit of lung tissue and the peripheral pulmonary arteries present thicker smooth muscle layer[52,53]. All these morphological variations contribute to the development of pulmonary hypertension. When babies that present pulmonary hypertension are born the pressure in their right atrium is relative high compared to the left atrium's leading to a persistent fetal circulation[54]. Extracorporeal Membrane Oxygenation (ECMO) is used to alleviate pulmonary hypertension after birth.

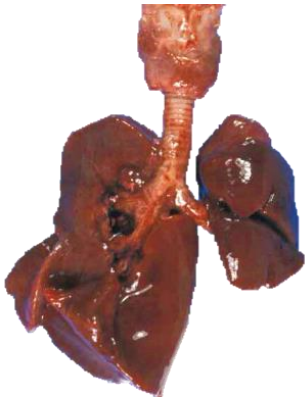

Figure 14. Hypoplastic lungs **[13]**

5.3 PRENATAL DIAGNOSIS AND PROGNOSIS

The prenatal diagnosis of CDH is mainly based on the visualization of abdominal organs into the thorax during routine ultrasound screening. The average gestational age for the diagnostic is 24 weeks. The visualization of the fluid-filled bowel or the stomach bubble in the thoracic cavity is highly diagnostic[55].

When the hernia is in the right side of the diaphragm is more difficult to diagnose because it is difficult to distinguish the lung tissue from the liver[9]. Sometimes the diagnosis of CDH can be missed due to the intermittent herniation of abdominal organs. In 80% of the CDH cases there is an excess of amniotic fluid. When the stomach herniates into the chest, the esophagus is compressed and the fetal

swallowing of amniotic fluid is obstructed leading to polyhydramnios[48]. The diagnosis of CDH can be confirmed by a chest X-ray, which will show part of the intestines in the chest.

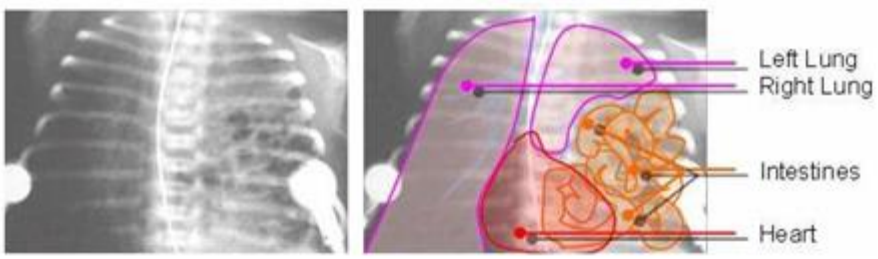

Figure 15. X-ray image showing herniated intestines compressing the lungs **[14]**

The prognosis of fetuses with isolated congenital diaphragmatic hernia depends on the severity of lung hypoplasia and pulmonary hypertension. The most widely sonographic predictors of postnatal outcome are the lung-to-head ratio (LHR) and the liver position[9,56,57,60,73]. To obtain the LHR the length and the width of the right lung are measured at the level of the four-chamber view of the heart and both values are multiplied. This is divided by the fetal head circumference. Liver herniation ("liver up") predicts poor outcome, the survival is 43%, whereas if the liver is not herniated ("liver down"), the survival is 93%[58]. In fetuses with intrathoracic herniation of the liver, the measurement of the LHR at 22 to 28 weeks of gestation, is a useful survival predictor[59]. Low LHR indicates that the lungs are extremely underdeveloped. Therefore fetuses with a LHR<1 have not almost chances of survival after birth and they are candidates for prenatal intervention. Those with a LHR>1, even though they will experience respiratory difficulties after birth, they will survive with postnatal therapies.

5.4 HOW CAN CDH BE TREATED?

Babies with CDH are usually delivered at 38 week of gestation and the delivery has to be planned ahead of time. The postnatal care consists of stabilization and resuscitation, respiratory support, use of medication to assist lung function and blood circulation. Once the baby is stabilized, usually within the first 10 days of life, the diaphragmatic hernia is repaired[61]. The abdominal organs are moved back to the abdominal cavity and the hernia is closed[62]. This is an efficient treatment for those fetuses with LHR>1 and no liver herniation, who are very likely to survive. However, most of the fetuses with severe CDH, LHR<1 and liver lifted upwards into the thorax, will die after surgery due to pulmonary hypoplasia and pulmonary hypertension[61,63]. Their lungs do not have enough size to provide sufficient oxygen intake during the first days of life. Therefore, it is necessary to improve the outcome of these severe cases of CDH improving lung development before birth.

For several years the benefits of prenatal diaphragmatic hernia repair were studied in the CDH fetal lamb model. In the late 80s the open fetal surgery was applied to humans[4,71,72]. It was observed that after the in-utero surgical repair, lung growth improves and therefore the survival rate increases. However, preterm labor and premature rupture of membranes were usual due to the large uterine incision required to access to the fetus[5,65]. Furthermore, most of the fetuses had a significant morbidity, especially permanent injuries in the CNS. Apart from that, this surgical procedure could just be performed in individuals with no liver herniation. It is not possible to repair “liver up CDH” in utero, because returning the liver back to the abdomen obstructs the umbilical venous return resulting in fetal death[13,66,67]. Therefore, due to the later reasons, researchers started looking into new less invasive techniques that could trigger lung growth in utero.

Several studies in animal models and in human fetuses have shown that utero temporary tracheal occlusion using fetoscopic techniques triggers pulmonary growth, reversing the pulmonary hypoplasia and hypertension[20,64,75].

Initially fetoscopic tracheal occlusions were done by laparoscopy. Through very small uterine incisions occlusive clips or tracheal foam plugs were used to obstruct the trachea[68.70]. Even though reduction of pulmonary hypoplasia was observed after the procedures, some of the patients ended up with permanent injuries in the laryngeal nerve[69]. For the last decade occlusive balloons have been used for the endotracheal occlusion. By using the balloons not only neck dissection and external clipping are avoided, also the tracheal changes experienced in fetuses after surgery are not significant with no damage in the cartilage[76,78].

6 FETOSCOPIC ENDOTRACHEAL OCCLUSION

Individuals with severe CDH are the right candidates for prenatal tracheal occlusion, the surgery will increase considerably their chances of survival after birth. The existence of liver herniation and a LHR<1 are the criteria used to select the patients who are suitable for the surgical intervention, because they are the ones with worst prognosis[59]. Once the balloon is detached in the trachea, the blockage of the airways will produce lung fluid accumulation in their lungs triggering lung growth[12,13]. When they are born, their pulmonary hypoplasia and pulmonary hypertension is not that severe and they are likely to survive with postnatal therapies like respiratory and circulatory support.

6.1 SURGICAL INSTRUMENTS

6.1.1 Trocars and cannulas

Trocars are elongated, sharp pointed medical devices used to provide access to the uterus during the fetal surgery. The trocar has a sharp end which penetrates muscles and soft tissues facilitating the access to body cavities. The trocar is inserted in a cannula and this assembly is pushed through the skin incision. It goes through muscular tissues, membranes and other soft tissues until it reaches the body cavity where the surgical procedure is performed. In that moment the trocar is disengaged from the cannula and it is withdrawn, leaving the cannula in place. The cannula will be the accessing channel to the cavity for the surgical instruments[73,76,77].

Cannulas used in fetal surgery should meet some requirements. First of all, they should be readily sealable so than amniotic fluid leakage is prevented. Second, but not less important, it is essential that the cannula minimises leakage and membrane dissection in the area surrounding the passage of the cannula through the choriaminiotic membranes and uterine wall[79].

Figure 16. Flexible cannula loaded with a sharp trocar for insertion **[15]**

6.1.2 Fetoscopic sheaths and fetoscopes

One of the fetoscopic instruments used in minimal invasive fetal surgery are fetoscopes, which are flexible fiber-optic tubes with a tiny video camera and good quality light source[74,76,77]. Usually they are used within a fetoscopic sheath that acts as a protection and a guide for the scope. Sometimes the sheath is slightly bended so that the fetoscope has an appropriate angle to reach the target. The most common type of sheaths are double lumen tubes, loaded with a fiber fetoscope and the balloon occlusion system, consisting of a loading catheter with a detachable balloon on the tip[76,74,80].

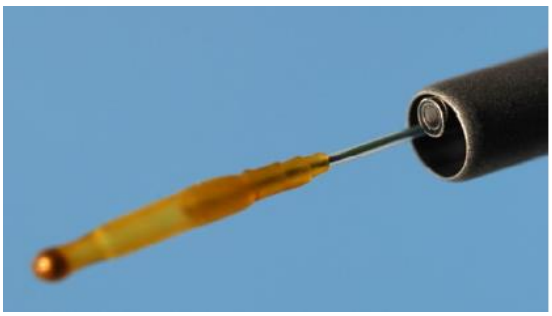

Figure 17. Sheath loaded with fetoscope and deflated balloon **[16]**

6.2 ULTRASOUND MEDICAL IMAGING

6.2.1 What is ultrasound?

Diagnostic ultrasound, also called sonography is a medical imaging technology that uses high frequency sound waves to produce images of the internal structures of the body. The term ultrasound describes mechanical waves above 20kHz. For medical applications frequencies in the range 1-20 MHz are used[82-84]. Both generation and detection of ultrasound is done using crystal of piezoelectric materials. Ultrasound is produced by the reverse piezoelectric effect whereas the detection relies on the piezoelectric effect. Therefore, the same material can be used to produce ultrasound and to detect the echoes returning from the internal body tissues[85]. One of the most important parameters of the sound waves is the frequency, which determines how many waves are sent per unit of time and it depends on the thickness of the crystal used in the transducer. The thicker the transducer is, the lower the frequency is. High frequency allows to obtain high quality resolution images but, the penetration of the sound waves is lower[85].

When the high frequency sound waves reach a tissue or fluid in the body, they will be attenuated and penetrate the structure. At tissue interfaces ultrasound waves are reflected. The intensity of the returning echo depends on the difference in acoustic impedance between the two structures traversed by the beam. Those echoes return back into the transducer and the ultrasound image is produced. The brightness of the image depends on how strong the reflections are[86].

The acoustic impedance (Z) measures how ultrasound traverses a tissue and it depends on the density of the medium (p) and the velocity of the ultrasound in that medium (v).

$$Z = p \cdot v$$

The greater the difference between the acoustic impedances in both tissues is, more echoes are reflected and the brighter the image is[86].

6.2.2 Ultrasound in minimal fetal invasive surgery

Ultrasound can be also used for tracking the position of surgical instruments during minimal invasive fetal surgery[87]. It is considered a safe imaging technology, because neither the fetus nor the mother are exposed to ionising radiation. However, the use of real time ultrasound guidance requires great surgical skills and a good coordination between the eye and the hand. During FETO ultrasound is used for a better guidance of the fetoscope and to assure the correct positioning of the balloon[76,77,80,81].

6.3 SURGICAL PROCEDURE

The introduction of the balloon is usually done at about the 26-28 week of gestation[13,76,89]. During the surgical procedure the mother is under epidular or local anesthesia and the fetus is sedated[13]. The position of the fetus is checked by ultrasound examination. If necessary, the fetus is manipulated so that the access to the trachea is easily achieved[13,76]. A flexible cannula loaded with a trocar is inserted through the skin incision into the uterus and directed toward the fetal mouth. In that moment the trocar is withdrawn and a fetoscopic sheath, equipped with a fiber optic fetoscope and a catheter with a detachable balloon on the tip, are inserted through the cannula. The endoscope is inserted in the fetal mouth and advanced down into the pharynx, then the larynx and finally through the vocal cords to the trachea[76,81,89].

Once the fetoscope is in the carina, where the bronchial trees bifurcate, the balloon is inflated with an isotonic solution and is left in the baby's trachea blocking the airways. High-resolution ultrasound imaging technology is used to ensure the proper positioning of the balloon[76,77,80,81]. As mentioned anteriorly, occluding the trachea of the fetus would prevent the egress of the lung fluid causing an increase in intrapulmonary pressure and lung growth is triggered. The abdominal organs that are in the chest will gradually move back into the abdominal cavity. Ultrasound examination is performed every 1-2 weeks to check that the occlusive balloon is in

the correct position and to monitor lung growth[89]. Approximately after 8 weeks the balloon is removed either by a secondary fetoscopic procedure or a ultrasound-guided puncture.

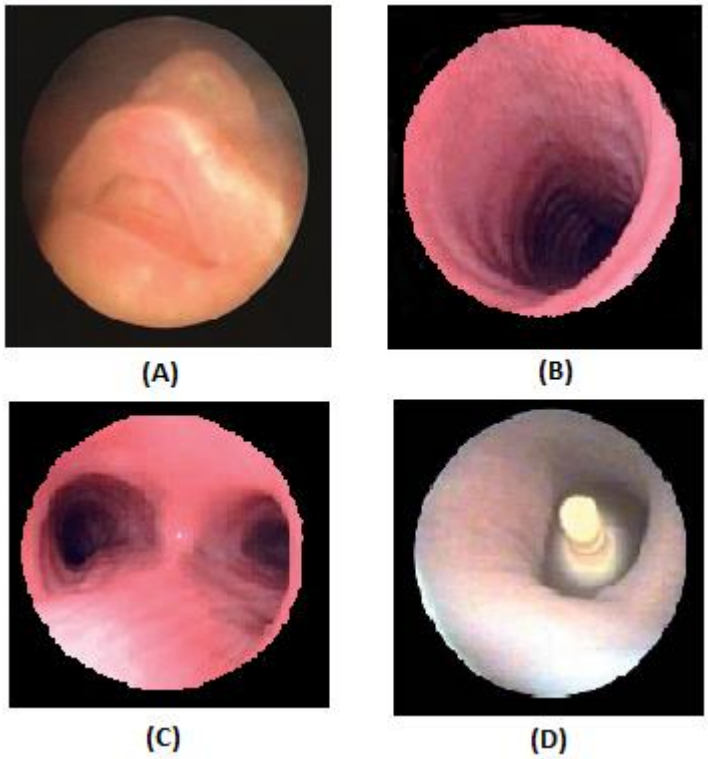

Figure 18. Fetoscopic images during FETO (A) Fetal mouth (B) Fetus trachea (C) Fetus carina (D) Inflated and detached balloon left into the trachea

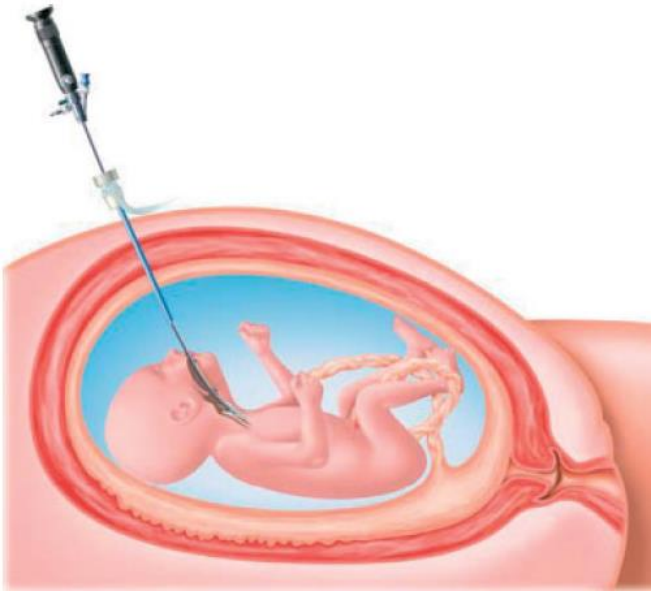

***Figure 19. Schematic drawing of FETO using a detachable balloon* [17]**

6.4 SIDE EFFECTS OF FETO

The use of a rigid fetoscope makes necessary fetal manipulation during the surgery so that the neck of the fetus is hyperextended and the introduction of the fetoscope in the trachea can be achieved. These changes of fetal neck angle produces stress on the cervical vertebrae of the fetus and the neck hyperextension may result in fetal discomfort and distress[90]. Moreover, great surgical skills are required to perform the surgery. The surgeon must have an excellent eye-hand coordination. The insertion of the fetoscope into the trachea might damage some delicate tissues of the fetus, such as the vocal cords.

FETO is a minimally invasive surgical procedure. Usually there are not serious complications for the mother. The results of leading medical centers having significant experience with FETO show a high rate of preterm premature rupture of membranes (PPROM), rupture of membranes before the 37th week of gestation, with vaginal leakage of amniotic fluid after intrauterine fetal surgery using a 3-mm sheath[75]. Sometimes the leakage stops and the pregnancy continues normally until

delivery but, unfortunately in some other cases the membranes rupture results in preterm labor and delivery.

Studies have shown that using ultrathin fetoscopic equipment in combination with real time 3D ultrasound may reduce the risk of PPROM. The dimension of damage to the amniotic membrane is an influencial factor in the rate of PPROM affer the fetoscopic surgical procedure[90].

Animal experiments have shown that the balloon does not cause any important damage to the trachea. However, some babies present a widening in the trachea but, it is uncertain what the reason of that change of size is[64].

7 OBJECTIVES

In FETO, the introduction of the rigid fetoscope into the trachea requires the hyperextension of the fetal neck which may cause cervical vertebrae stress. This is considered one of the most relevant drawbacks of the surgical procedure. Surgeons and health professionals are really concerned about the effects that the hyperextension of the cervical vertebrae might cause in the fetus' neck. To date, neither doctors nor engineers, have studied experimentally, the variation of the neck angle during FETO. As an engineer, I really think that the analysis of the cervical vertebrae extension during the surgery is a very interesting and challenging work. It will provide useful data and results that will be extremely helpful and determinant for future possible improvements and approaches in minimal invasive fetal surgery instrumentation. Due to the above mentioned reasons, the present project's objective is to determine and analyse the fetus' neck angle during the FETO procedure, when a rigid fetoscope is used.

8 MATERIALS AND METHODS

8.1 MODELS

As mentioned before, FETO surgery is usually performed at 26-28 weeks of gestation. For the experiments a baby doll and a phantom respiratory tract were used so that a metal tubing could be introduced into the trachea through the baby's mouth. It is was extremely important and essential that their dimensions were quite similar to those of fetuses of 27 weeks, which is the mean gestational age of the babies when they undergo surgery. Hence, the first step was to look into the dimensions of the fetus, the fetus' trachea and the upper respiratory tract at that gestational age. In Section 8.3 it is explained what fetal features were used to determine the gestational age of the phantom baby and how they were measured making use of ultrasound

imaging technology. Section 8.4 provides detailed information about the studies and equations used to estimate the dimensions of the different parts of the respiratory tract.

8.2 IMAGING SYSTEM

Making use of ultrasound imaging it was possible to obtain good quality images of fetus' head, neck and chest to make the measurement and analyse the variation of the angle neck since the rigid fetoscope is inserted into the mouth until it reaches the trachea, where the balloon is inflated and detached. The ultrasound machine used was the model JustVision 400 from TOSHIBA. It can operate at three different centre of frequencies. The lowest and the highest frequencies, are 3.5 MHz and 9 MHz respectively.

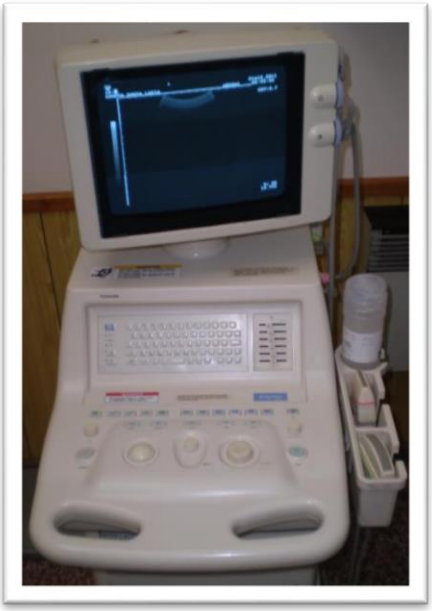

Figure 20. TOSHIBA JustVision 400 ultrasound equipment

It allows to obtain images in different modes of ultrasound. For this application B mode images, also known as brightness mode, were obtained. In this mode of ultrasound the 2D image represents internal tissues and organ interfaces. The pulses

are sent by the transducer passing through tissue, organs and more internal body structures. The image is constructed from the echoes which are reflections of the pulses at tissue boundaries. The brightness of the image at each point depends on the strength of the reflection[98].

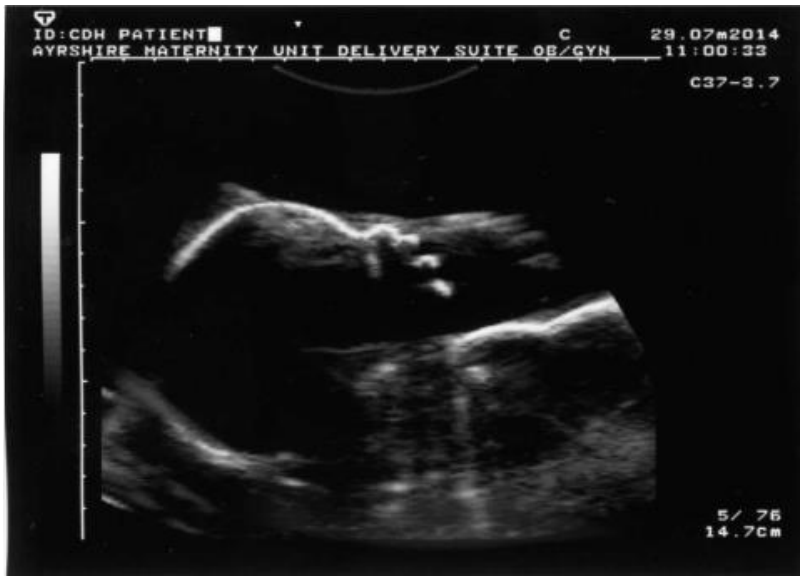

Figure 21. B mode ultrasound image

The ultrasound machines is equipped with two transducers but the Toshiba PVG 366M was chosen for this application because a wide field of view was required. This transducer is a convex probe and it has a frequency range of 3-3.75 MHz.

Figure 22. Toshiba PVG 366M transducer

The principal objective was to obtain images with the best possible quality and to do so it was necessary to optimize the images. First of all obstetrics and gynaecology was set as the medical application. The gain, which determines the amplification of the sound waves and therefore the brightness of the ultrasound image, was adjusted to accentuate the appearance and border of the internal structures. Gain is measured in a scale ranging from 60 to 100. For this application a gain of 80 was set. Echoes that return from deeper tissues will be more attenuated because they have to pass through more structures. Hence, the intensity of the image of those structures will be much lower than for closer tissues. Time gain compensation allows to overcome that problem allowing to amplify echoes that are reflected from deeper tissues to make the image more uniform. The machine has a group of 6 TGC controls which allow to adjust the gain in specific areas of the image. There is a parameter called Imaging Processing that controls the contrast and the greyscale of the image. It is measured in a scale from 1 to 8. The user manual of the ultrasound machine suggests to set it in the range 5-6 for abdominal applications, providing smoother images with more grayscale.

Figure 23. Ultrasound image settings

During this academic year, I learned about ultrasound and its physics principles but I had never used an ultrasound machine before. The first task that I had to face was to learn how to use it from zero. Having the theoretical knowledge and understanding of how ultrasound technology works helped me to understand more easily what the images showed. However, I had no skills when it came to use the machine, to adjust the parameters to optimise the image quality and I did not even know how I had to position the transducer to obtain images in the different planes. The ultrasound machine available in the laboratory is quite old and there was no user manual so I had to learn how to use it by myself. It would have been much easier if I had had some help but it was a challenge for me what motivated me. Making use of a baby doll submerged into a water tank I practiced and learned not only how to obtain images in different planes and make measurements but also, how to interpret the images and identify in detail the structures that are represented in them.

As mentioned before, one of the objectives was to obtain good quality ultrasound images. Once I was able to capture good quality images it was time to think how to obtain digital images from the ultrasound machine so quality was not decreased. The software Honestech HD DVR 2.5 was used to transfer the ultrasound images from the ultrasound machine to the laptop

8.3 FETAL BIOMETRIC FEATURES

The gestational age may be determined by ultrasound biometric measurements, assuming that the fetus is growing normally. The gestational age can be estimated during the second and third trimesters by measuring multiple biometric features. The most commonly used, due to its accuracy, are the biparietal diameter (BPD), head circumference (HC), abdominal circumference and femur length[91,92]. It is common to make at least two measurements to determine the gestational age. For the present project the BPD and the HC were measured. By doing this, it was checked and

confirmed that the phantom fetus used for the project has approximate dimensions of those of the 26-28 week real baby.

8.3.1 Biparietal diameter

The BPD is the transverse diameter of the fetus head measured in the axial plane that transverses the septum pellicidum, the third ventricle and the thalami[91,92]. To obtain the image in that plane, the transducer must be placed perpendicular to the central axis of the head. The diameter is measured from the outer edge of the proximal skull wall to the inner edge of the distal skull wall[93].

The ultrasound image shown below shows the BPD measured in the phantom baby. The ultrasound machine allows to measure the BPD and it gives automatically the gestational age of the baby according to the BPD value. In this case the BPD is 66.4 mm, corresponding to 27 weeks gestational age.

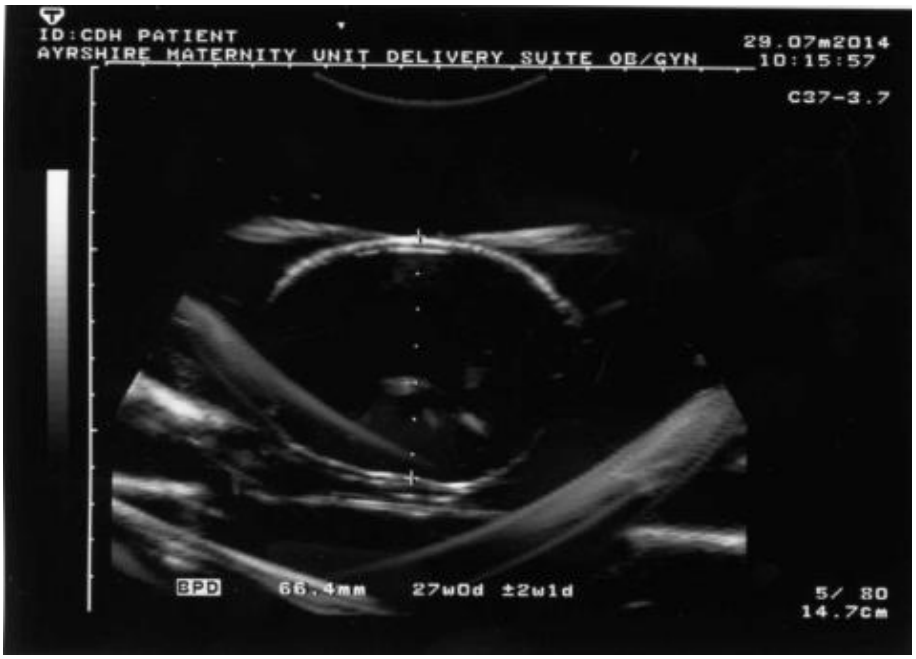

Figure 24. Biparietal diameter measurement using ultrasound

This transversal view of the fetus head is achieved if the transducer is positioned as *Figure 25* shows:

Figure 25. Transducer position to obtain images in the axial plane

8.3.2 Head circumference

The head circumference is the perimeter of the fetus' head in the axial plane. The calculation of the perimeter of an ellipse is not an easy task, in this case the following equation was used:

$$\mathrm{HC} = \frac{\pi}{2}\,(\mathrm{BPD} + \mathrm{OPD})$$

Being OPD the occipitofrontal diameter measured in the axis plane from the leading edge of the frontal bone and the outer border of the occiput[94].

In the following image the OPD measurement is shown. It was measured in the same plane as the BPD.

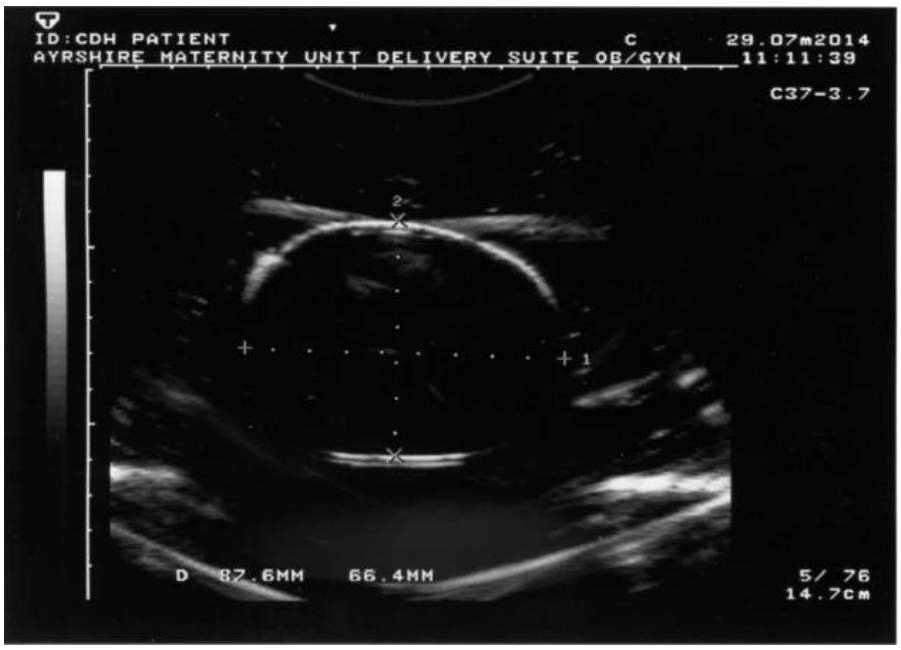

Figure 26. BPD and OPD measurement using ultrasound

$$\mathrm{HC} = \frac{\pi}{2}\,(66.4 + 87.6) = 241.9\,mm$$

According to the table shown in *Figure 48* in Appendix 1, for that value of HC the baby would be between 25 and 27 weeks, confirming the gestational age obtained in terms of BPD.

8.4 FETAL RESPIRATORY TRACT DIMENSIONS

For the experiments, a phantom silicone tubing respiratory tract, including mouth, pharynx, larynx, trachea and bronchial trees, was used. Even though, it was just planned to use a phantom trachea and not the upper respiratory tract, it was necessary to develop a tubing from the mouth of the baby until the bronchial trees. The reason was that, working just with the trachea it was not possible to attach it steadily to the baby. Apart from that, the tubing used, which starts at the entrance of the mouth, worked as a guide for the rigid sheath. From the entrance of the mouth until the carina the rigid sheath followed the shape of the tubing, which has similar

dimensions and form to those of the upper respiratory tract. The dimensions of the tubing were chosen considering the real dimensions of the fetus' trachea at the 26-28 week of gestation. According to Michal Szpinda et al.[95] the length of the trachea, measured from the first tracheal cartilage until the carina, can be calculated using the following logarithmic equation:

$$LT = -65{,}098 + (28{,}796 \cdot ln(GA))$$

Being LT the length of the trachea (mm) and GA the gestational age (weeks).

The length of the 27 weeks fetus' trachea is 29.8089 mm, value that was approximated to 30 mm.

Michael Szpinda et al. provide also an equation to estimate the internal cross sectional area of the trachea depending on the gestational age. The equation is as follows:

$$CSA = -3{,}562 + 0{,}352 \cdot GA$$

Being CSA the internal cross sectional area of the trachea (mm^2) and GA the gestational age (weeks).

The trachea of a 27 weeks fetus, the cross sectional area is 5.942 mm. Making use of this value, the internal diameter of the trachea can be easily calculated.

$$D = \sqrt{\frac{CSA}{\pi}} \cdot 2 = 2.7506\, mm$$

Even though the trachea is funnel shaped, having an upper end wider than the lower one, the internal diameter has been considered uniform, 2.75 mm. It was not possible to find silicone tubing with internal diameter of 2.75 mm, therefore tubes of 3 mm were used.

The last parameter that was calculated was the length of the bronchial trees. In this case Michael Spzinda et al. [94] provide the following equation:

$$LBT = -10{,}756 + 4{,}86 \cdot ln(GA)$$

Where LBT is the length of the bronchial trees (mm) and GA is the gestational age (weeks). According to that equation the bronchial trees of a 27 weeks fetus are 5.2618 mm long.

Once the dimensions of the trachea were known, the next step was to determine the approximate length of the oral cavity, the pharynx and the larynx. Even though an extensive research was done, it was not possible to find a study which provide equations to determine the dimensions of the fetal mouth in terms of gestational age. Regarding to the pharynx and the larynx, the length of both structures were calculated according to the equations provided by Liberty G. et al.[97]. By means of 2D and 3D ultrasound they evaluated the structure and the development of the pharynx and the larynx of fetuses. The following equation was used to determine the length of the pharynx:

$$\mathrm{PH} = 0.071 \cdot \mathrm{GA} - 0.34$$

Being PH the pharynx height and GA the gestational age. The value obtained for a 27 weeks fetus was 1.577 mm. The pharynx is divided in three parts: the nasopharynx, oropharynx and laryngopharynx or hypopharynx.

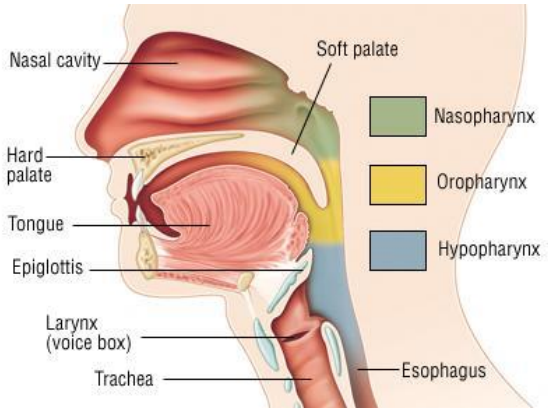

Figure 27. Parts of the pharynx **[18]**

In this case, just the oropharynx and part of the hypopharynx would be included into the mimic respiratory tract. However, the total length of the pharynx was considered.

The possible errors induced are almost insignificant due to the small dimensions of the structure. Moreover, it was no possible to determine the length of the oropharynx and know what percentage of the laryngopharynx was included.

In terms of the larynx, it is 1.264 mm long in a fetus of 27 weeks according to the equation:

$$LH = 0.062 \cdot GA - 0.41$$

Where LH is the heigth of the pharynx and GA is the gestational age.

Once the length of every structure was known, the mimic respiratory tract was developed. In terms of width, a silicone tubing with an internal diameter of 3 mm was used from the entrance of the mouth until the bronchial tress. Recall that the internal diameter of the tubing was chosen considering the width of the trachea of a fetus of 27 weeks. I decided to use a tube of constant width mainly because of two reasons. First, from my point of view, the most important parameter is the length of the respiratory tract because is the path that the fetoscope has to follow during the surgical procedure. Second, as the trachea is the structure that the fetoscope has to reach, I considered that the width of the tubing should be determined by the tracheal width.

8.5 EXPERIMENTAL SETUP

A phantom fetus with a mimic respiratory tract were used for the experiment. Previously, it has been proved that the baby used has similar dimensions to those of a 27 weeks fetus. The length and width of the respiratory tract used to mimic the real one have been calculated and justified in Section 8.4.

The first step was to construct the lower part of the respiratory tract that mimics the bronchial trees. From the entrance of the mouth until the carina, where the bronchial

trees bifurcate, the respiratory tract is basically a curved tube. The bronchial trees were attached to the lower part of the trachea introducing a strip of tubing into them, which was glued. The next figure shows the different parts that were put together:

Figure 28. Bronchial trees and trachea

The left bronchial tree is longer and it enters into the lungs less vertically than the right one. *Figure 29* shows the final assembly trachea and bronchial trees.

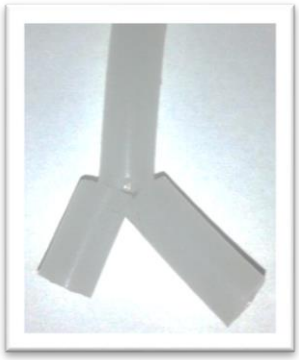

Figure 29. Phantom assembly trachea-bronchial trees

Attaching the respiratory tract to the baby was the next task. The top part of the silicone tubing was introduced into the baby's mouth. The rest of the tube was inserted through the fetus' neck down into the thorax. However, an unexpected problem arose, the tube tended to get close to the back part of the baby's body and the attachment was not stable enough. To encounter that problem, it was necessary

to fix the tubing approximately in the middle of the neck by means of a sponge and super glue. By doing this, the phantom respiratory tract was firmly fixed to the baby and the tubing stayed in the centre of the chest.

Figure 30. Phantom trachea and bronchial trees in fetus' chest

Figure 31. Respiratory tract fixed into phantom fetus

Figure 32. Phantom fetus with respiratory tract

During pregnancy the fetus is in the amniotic sac floating in the amniotic fluid. The main component of the amniotic fluid is water. Because of this reason, the baby was submerged into a plastic container filled with water, which resembles the fetus' environment in the uterus. As the baby is made of plastic and hollow, it was necessary attach it to the bottom of the container with Velcro tape because it floated moving to the surface.

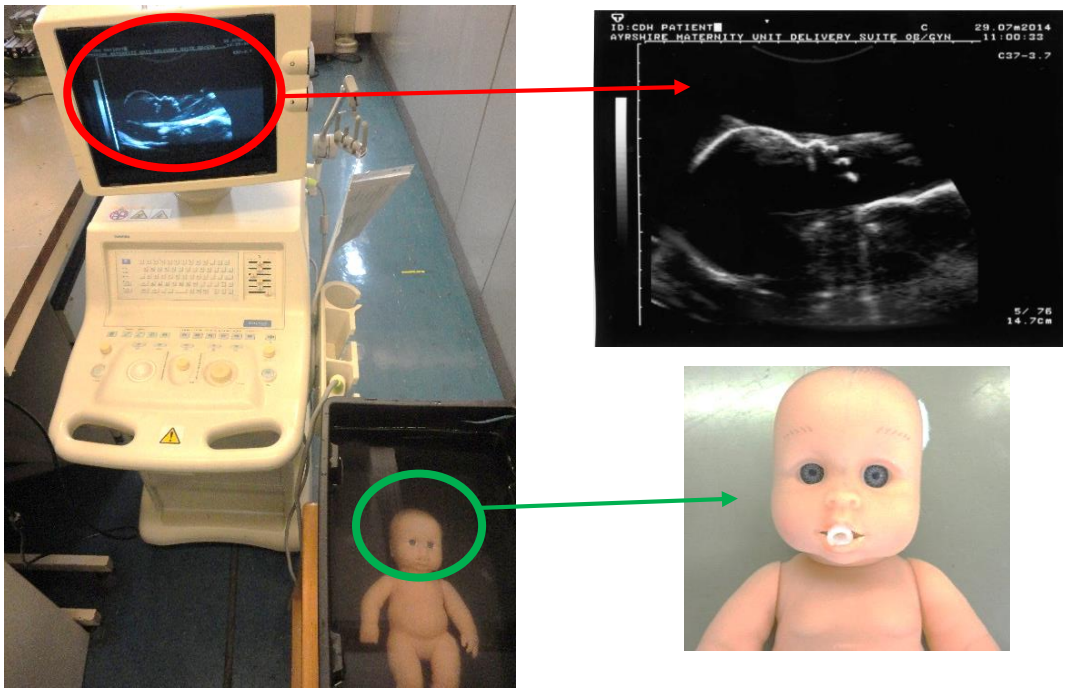

Figure 33. Ultrasound equipment and phantom fetus

A thin metal tubing was used to mimic the rigid fetoscopic sheath that is used in the real surgical procedure. It was introduced through the baby's mouth, inserted down into the pharynx, larynx and finally it reached the trachea. The sheath is rigid and most of the times it is slightly bended to facilitate its insertion into the trachea. However, it is not possible for the fetoscope to reach the trachea unless the fetal neck is hyperextended. During FETO it can be assumed that the neck is basically in two different positions. The fetoscope is introduced into the mouth through the lips [1], it is passed over the tongue [2] and it reaches the pharynx [3]. Throughout all this path it can be considered that the neck keeps in a constant position, Position 1.

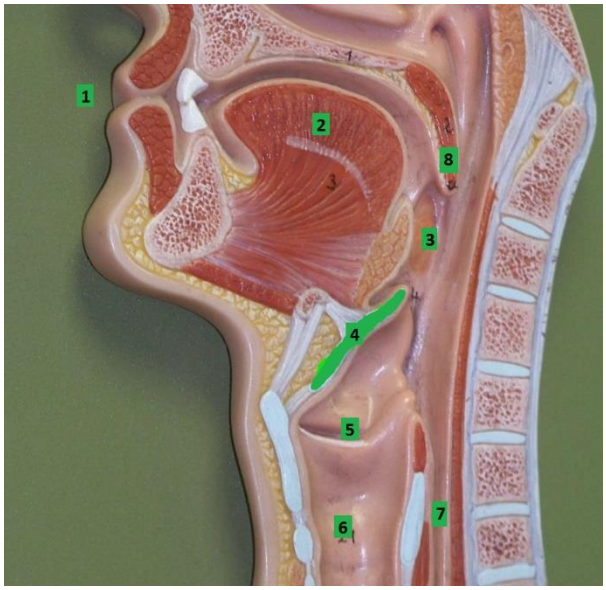

Figure 34. Human upper respiratory tract

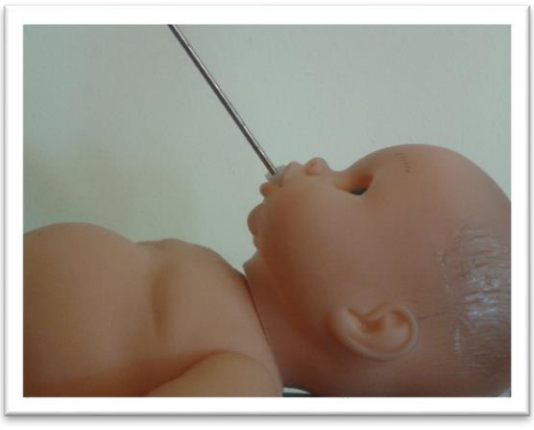

Figure 35. Rigid fetoscope inside of baby's respiratory tract for Position 1

From the beginning of the pharyns [3] the curvature of the respiratory tract changes dramatically. Every substance or object introduced into the mouth tends to pass through the esophagus [7]. In this case the fetoscope has to enter the trachea [6] which means that extreme hyperextension of the fetal neck is required because otherwise the fetoscope will enter the esophagus [7] and not the larynx [5].

When the fetoscope reaches the pharynx [3] the surgeon will make use of the fetoscope to force the neck hyperextension required. By doing so, the fetoscope can be advanced down into the epiglottis [4], passing through the larynx [5] and the vocal cords before entering into the trachea [6], where the detachable balloon is inflated and left blocking the airways for about 8 weeks. Even though in real surgery small variations happen, for the present project it has been considered that the position of the neck, from the moment the fetoscope is in the pharynx until it reaches the trachea, is constant. From now on that position will be called Position 2.

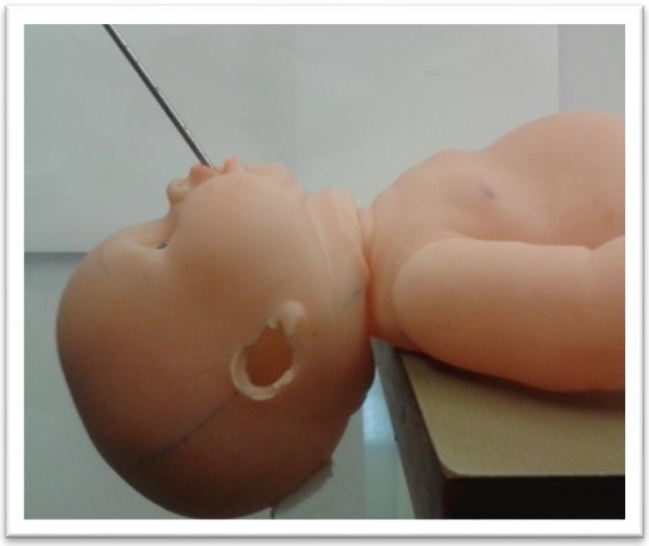

Figure 36. Rigid fetoscope inside of baby's respiratory tract for Position 2

To make possible the measurement of the neck angle, ultrasound images in the sagittal plane were taken for both positions, Position 1 and Position 2. It was a quite difficult task to obtain good quality images. Due to the fact that the rigid tube used is made up of metal, the ultrasound images showed a lot of reflections. Consequently

the quality of the images was not good enough and it was no possible to identify the fetal structures.

It is essential to bear in mind that the neck position was measured in the ultrasound images. Therefore, the results of this experiment rely completely not only on the quality of the images but also, on the correct visualization of fetus' chest, neck and head. Due to the above mentioned reasons, my skills using the ultrasound machine was a determinant and decisive factor in the project. Several training and practising sessions in the laboratory were needed before I was able to take images with enough quality.

To obtain images in the sagittal plane the transducer has to be positioned as shown in the picture:

Figure 37. Transducer position to obtain images in the sagittal plane

The next two figures show the best ultrasound images that could be obtained for both positons of the neck.

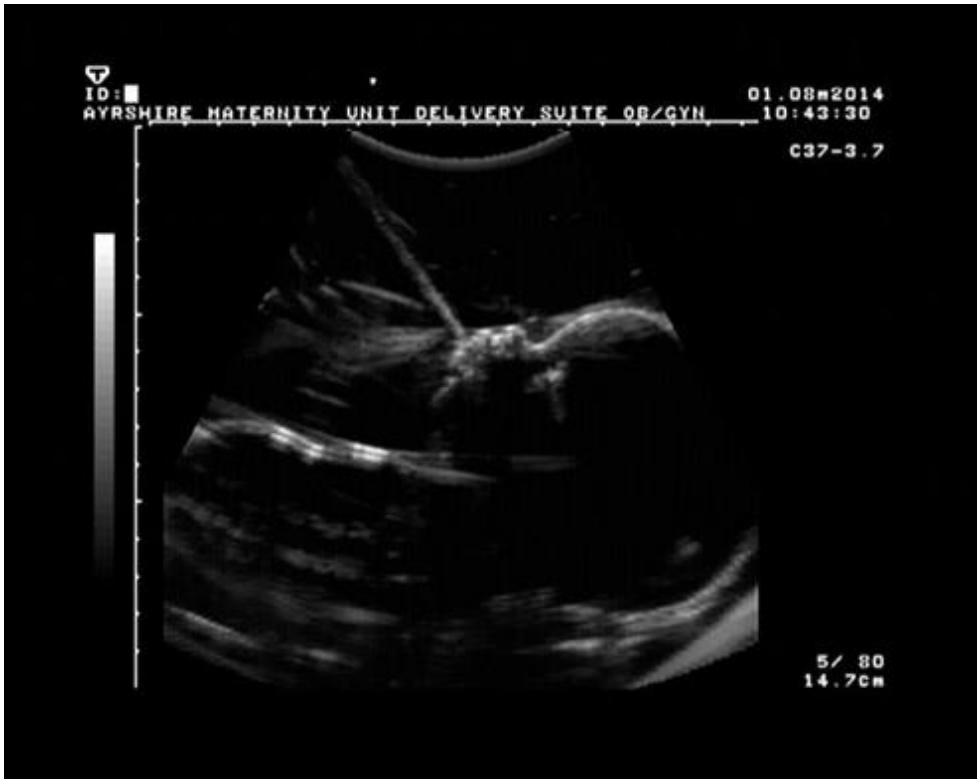

Figure 38.Ultrasound image for Position 1

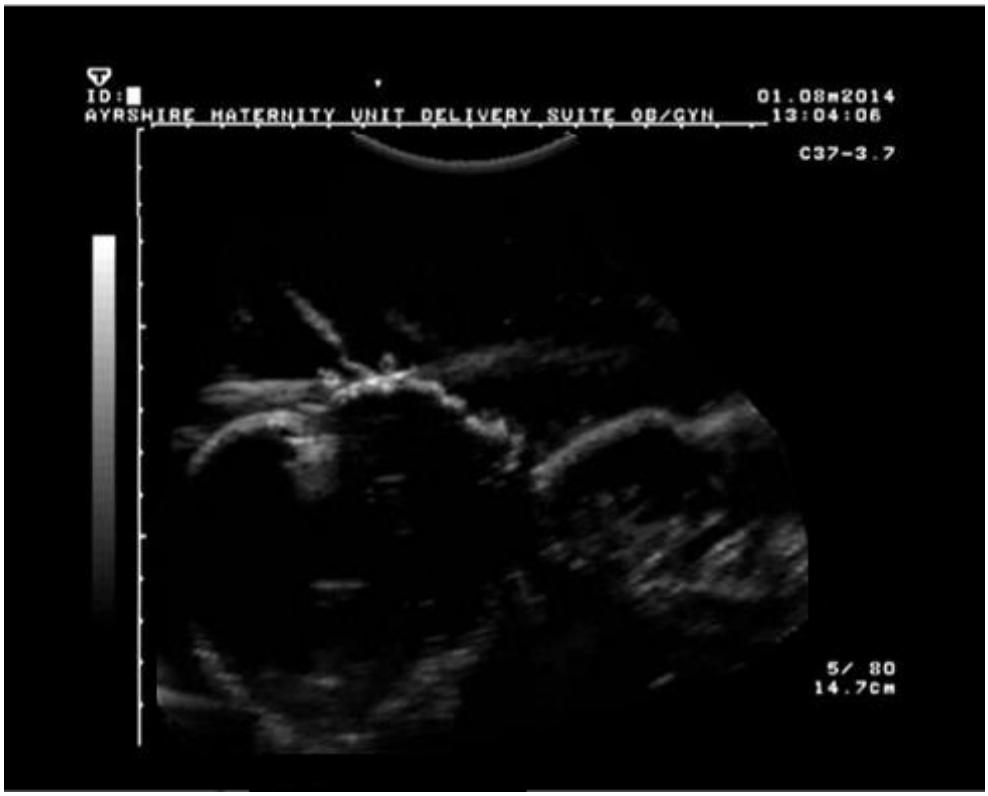

Figure 39.Ultrasound image for Position 2

During the first days of work with the ultrasound machine it was quite tricky for me to find the resemblance between the ultrasound images and the body that is examined. Therefore, I am fully aware that professionals who have no experience working with ultrasound imaging would find tough the interpretation of the images and the identification the structures shown in them. For this reason, in *Figure 40* and *Figure 41*, I tried to explain and clarify as much as possible the resemblance between the ultrasound image and the baby.

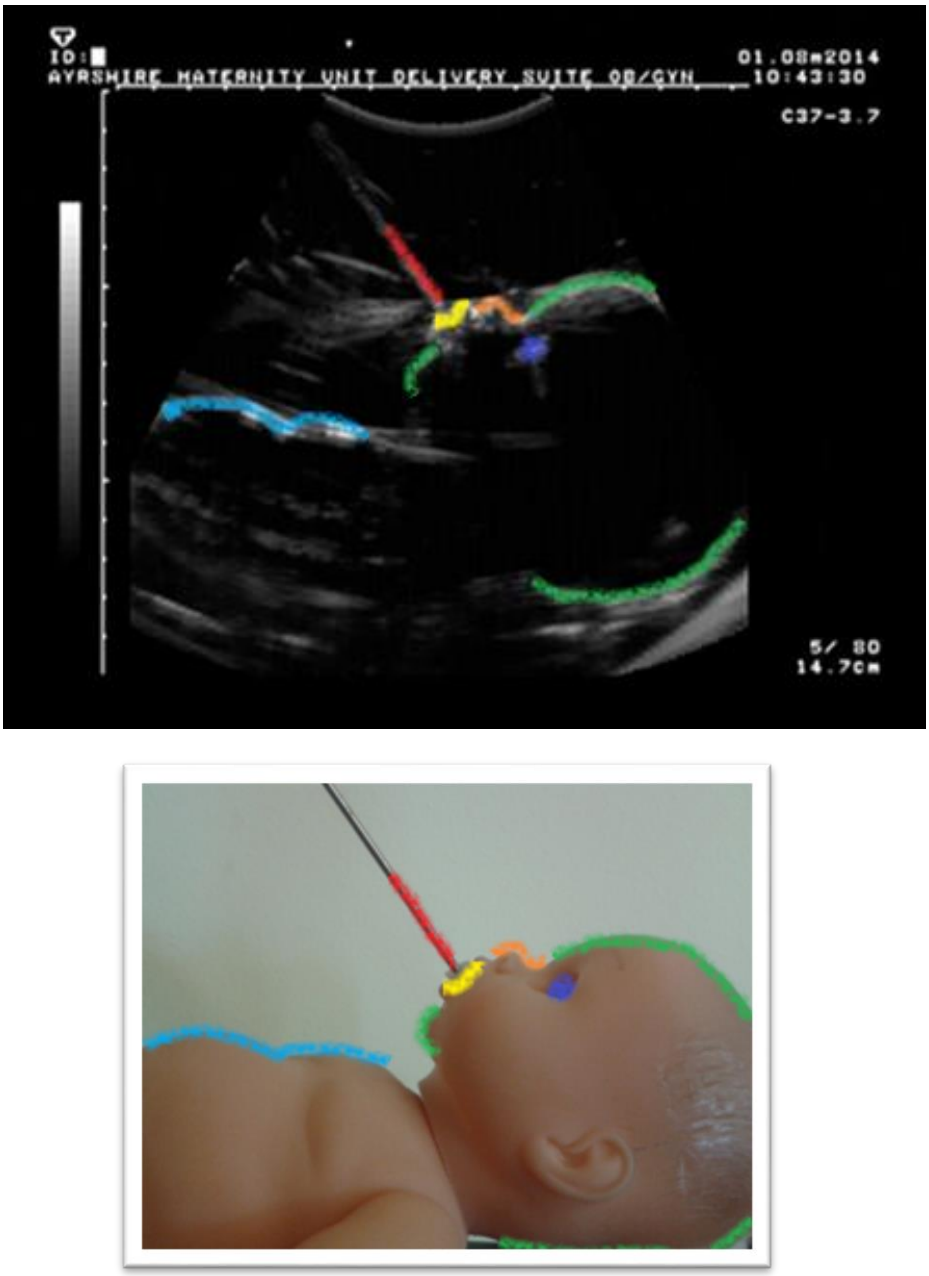

Figure 40. Identification of fetal structures in ultrasound image Position 1

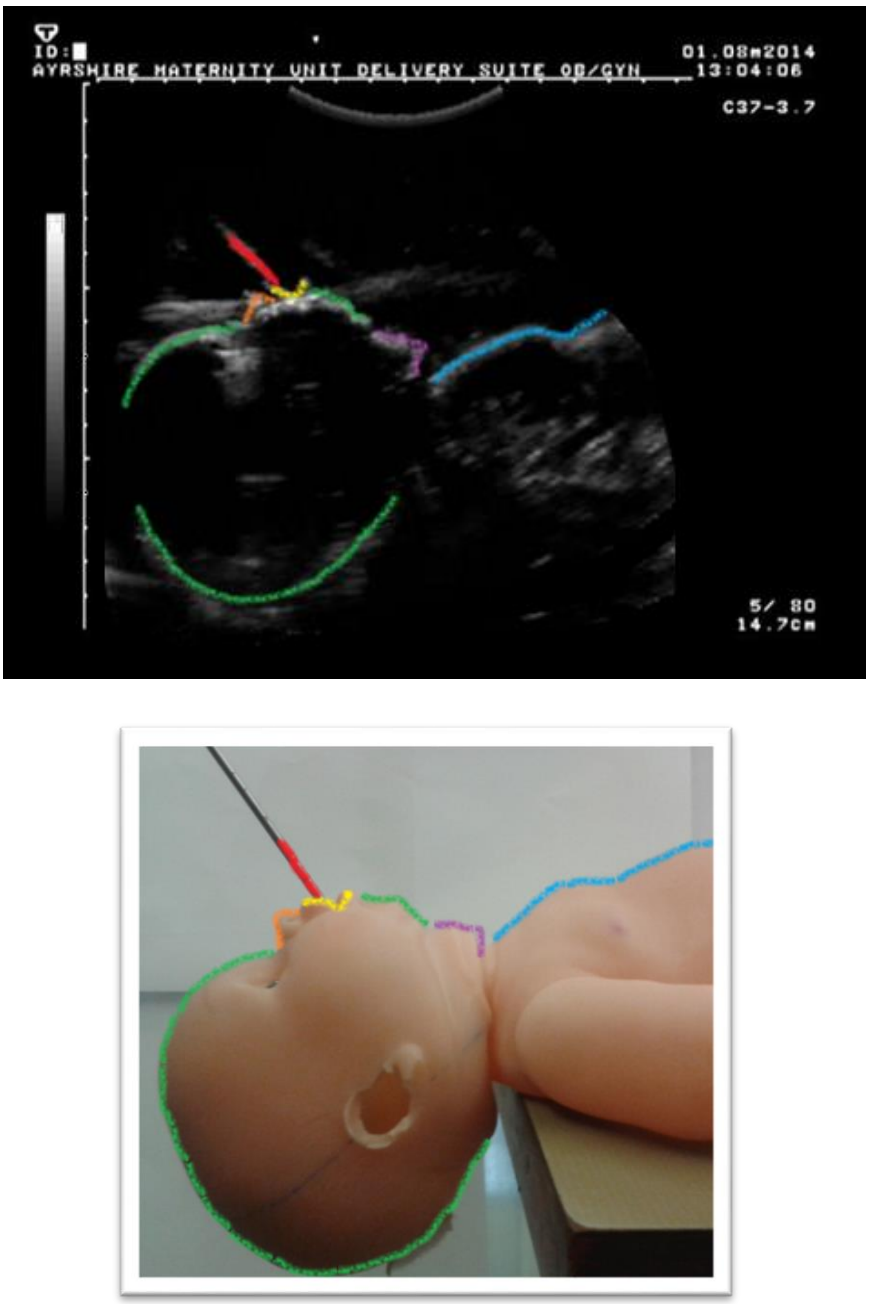

Figure 41. Identification of fetal structures in ultrasound image Position 2

I considered that it was also essential to obtain an image which shows the phantom respiratory tract into the fetus chest. The image was taken in the axial plane, positioning the transducer as *Figure 42* shows:

Figure 42. Transducer's position to obtain images in the axial plane

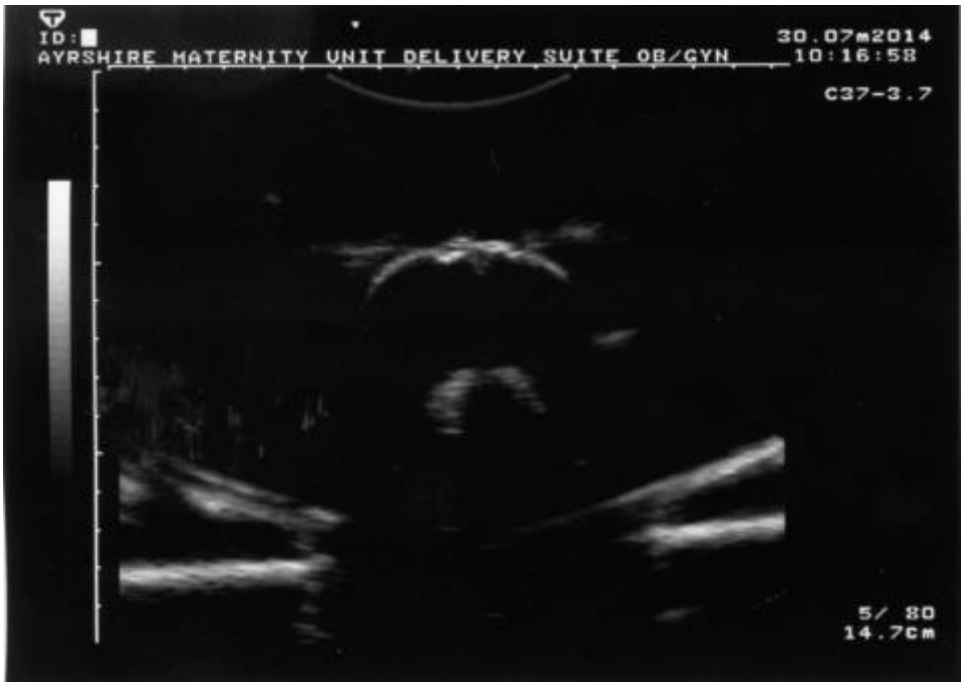

Figure 43. Phantom respiratory tract into fetal chest

8.6 METHODOLOGY TO MEASURE THE NECK ANGLE

The position of the cervical column was determined considering the rest of the spinal column as a reference. For the estimation of the angle of the neck some assumptions and considerations were made:

1. The position of the spinal column below the cervical section was considered to be constant and horizontal at every instant of the experiment. This assumption allowed to use that segment as a reference for the measurement of the change neck angle.

2. It was assumed that the cervical vertebrae was a unique segment. In other words, all the cervical segments rotated with the same angle around the same centre of rotation.

3. The position of the centre of rotation of the cervical vertebrae was estimated taken into consideration several factors.
    a. Its location is in the posterior area of the neck close to the vertebral column.
    b. The length of the phantom baby's neck was measured and the centre of rotation was situated in the middle of the neck height.

Angles are the point at which two lines intersect and a line is determined uniquely by two points. Therefore, the first step was to estimate the position of the points which define the lines.

As mentioned previously, the back of the baby was considered to stay horizontal and still throughout the experiment. The centre of rotation of the neck was considered to be the intersection of the back line and the neck line. To obtain the neck line another point was required. In this case I thought that using the middle point of the biparietal diameter was a logic and accurate method to determine the inclination of the neck.

The measurement were done using the ultrasound images but I preferred to use pictures of the baby to illustrate clearly how the points and the lines where determined.

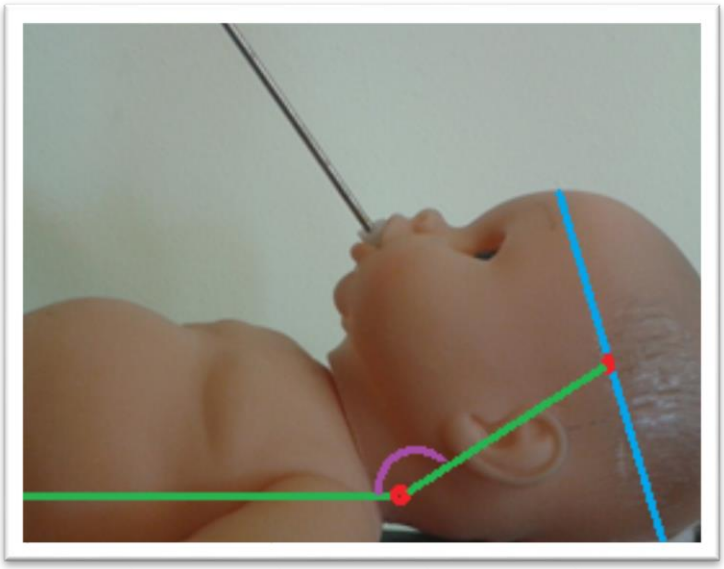

Figure 44. Determination of the neck angle

9 RESULTS

In order to obtain the most accurate and reliable data, the ultrasound images were printed in A4 size paper so that the measurements were more precise. Those papers are shown in Appendix 2.

9.1 POSITION 1

Since the fetoscope is introduced into the fetus mouth until it reaches the pharynx, in other words when the fetus is in Position 1, the angle of the neck respect the back of the fetus is about **140 degrees**. This value was obtained evaluating the angle shown in *Figure 45.*

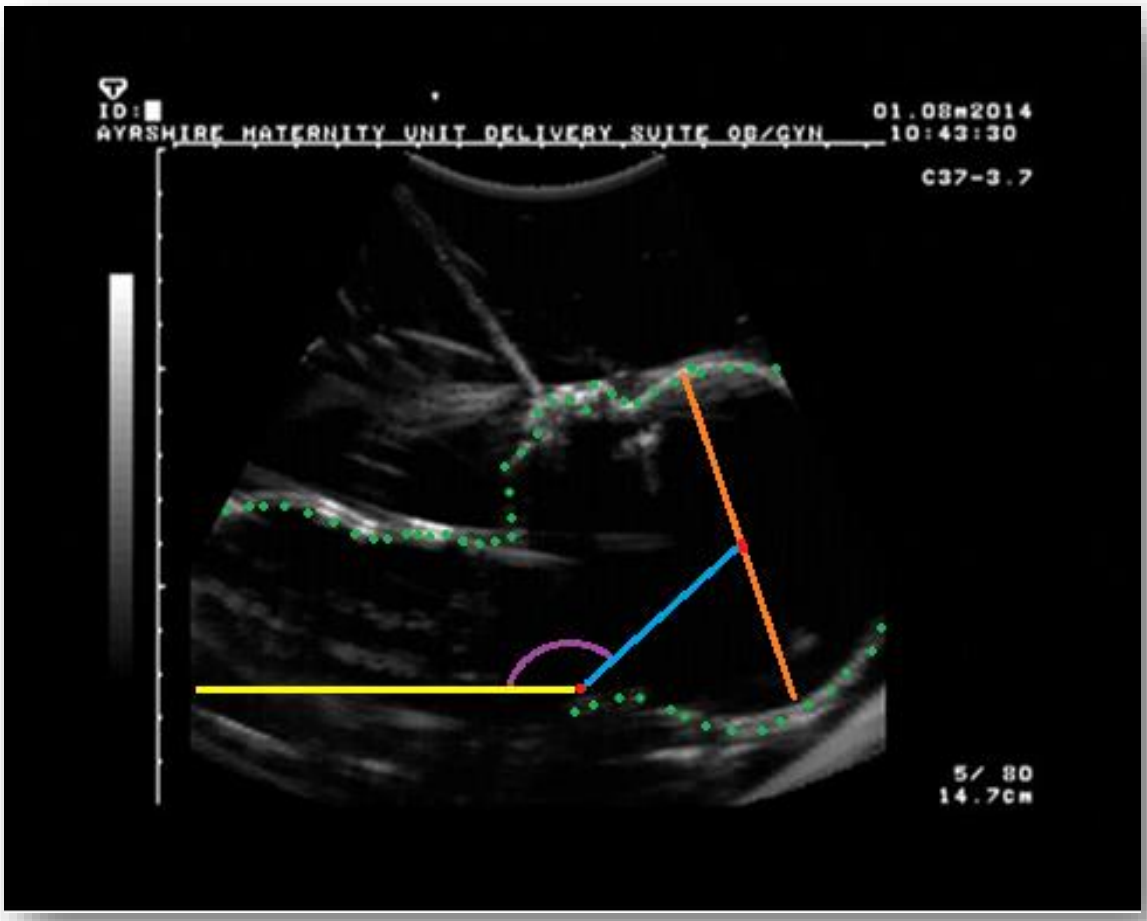

Figure 45. Angle in Position 1

9.2 POSITION 2

As explained previously, when the fetoscope is in the pharynx the neck has be forced to change of position drastically so that the surgical instrumentation can be advanced down into the trachea. For this second position of the neck, Position 2, the angle of the neck is approximately **190 degrees** according to *Figure 46*.

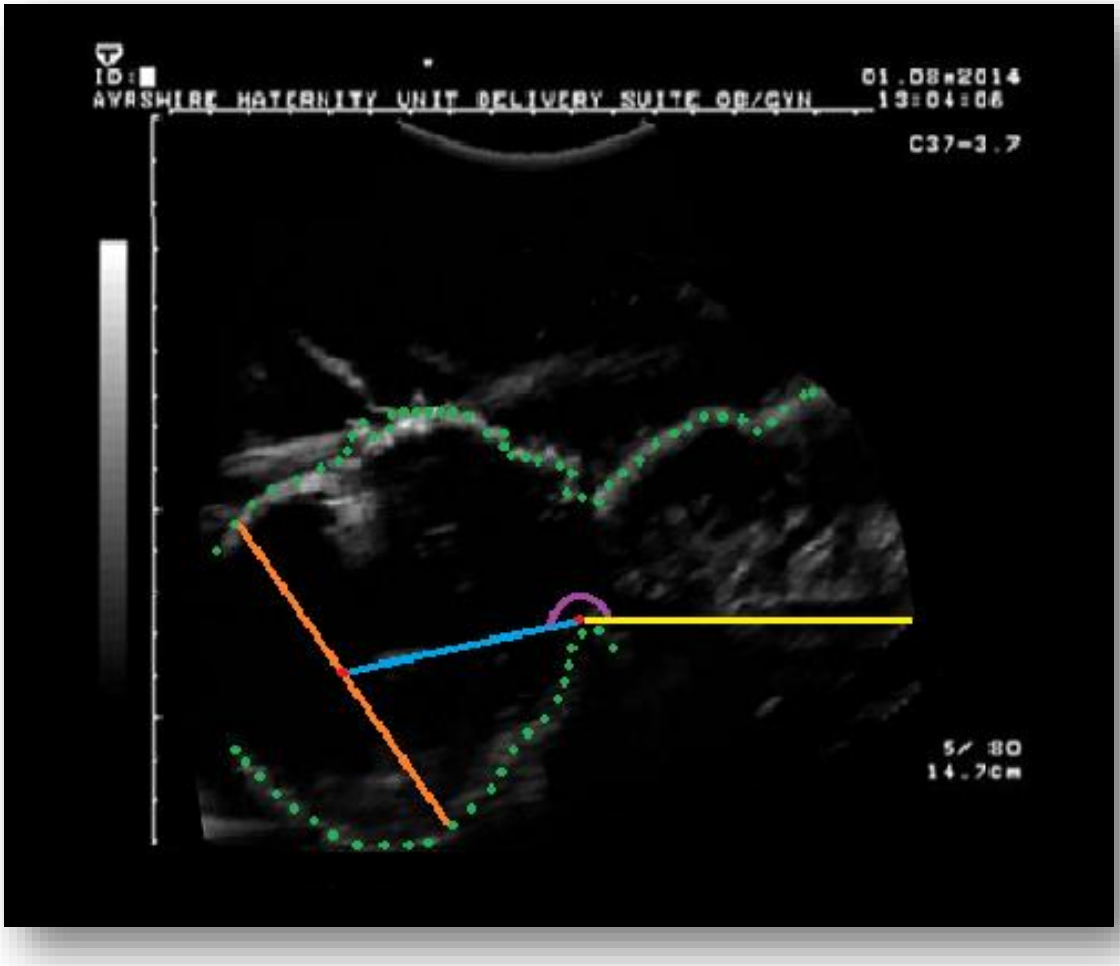

Figure 46. Angle in Position 2

Position Fetoscope	Position	Degrees
Mouth – Pharynx	1	**140**
Pharynx - Trachea	2	**190**

10 DISCUSSION

Experimental evidence have shown that Fetoscopic Tracheal Occlusion triggers lung growth, improves pulmonary function and neonatal survival. However, the surgical procedure has some complications. Usually the surgical instruments have a diameter that ranges between 3-4 mm. The use of these instruments can induce PPROM, being the most common complication of FETO. The size of the incision in the amniotic membrane is determinant for the risk of PPROM. Therefore, thinner fetoscopes have been developed so that the risk for the mother and the fetus decrease.

The use of rigid fetoscopes requires the hyperextension of the fetal neck during the procedure. There are many concerns about the possible cervical vertebrae damage and fetal distress that the unusual position of the head might cause. However, there are no previous studies that analyse and determine experimentally the extension that the neck undergoes during FETO. The results obtained have shown that the head undergoes an extension of about 50 degrees. Undoubtedly it is an angle variation of great magnitude. Even though the fetus is sedated during the procedure, that head hyperextension may create discomfort to the fetus. Moreover, it is essential to bear in mind how the head is forced to undergo that extension. Recall that when the fetoscope in the pharynx the surgeon forces the fetus to be in a hyperextended position so that the fetoscope can be advanced down into the trachea. Forces and pressure are applied in the lip palate upper maxilla and on the epiglottis of the fetus which leads to fetal damage.

Due to all these reasons, it is time to think about possible improvements and new approaches in fetoscopes for FETO procedure. The use of a flexible fetoscope would allow to perform the surgery without requiring any fetal manipulation. The tip of the steerable fetoscope is controlled by the surgeon using a thumbstick. When the flexible fetoscope reaches the pharynx the surgeon visualises the esophagus and the trachea and he manipulated the tip of the fetoscope into the trachea[14].

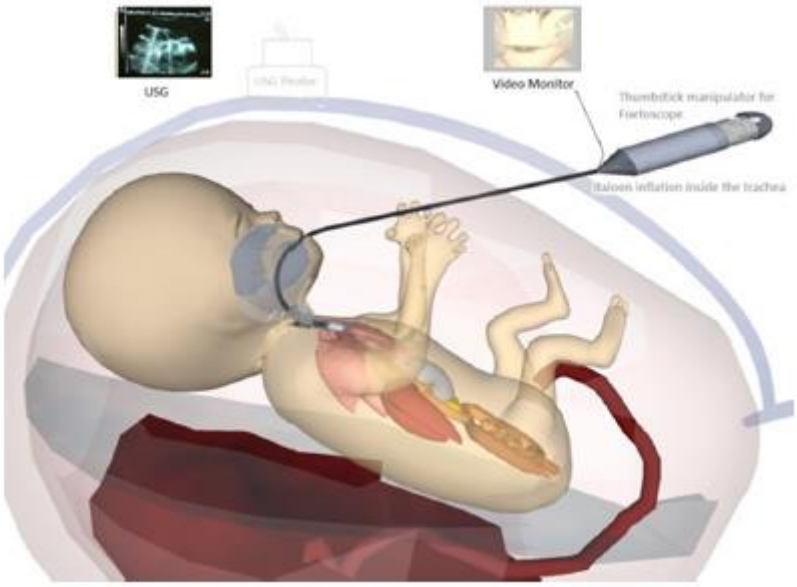

Figure 47. Introdution of steerable fetoscope into fetal trachea **[19]**

11 LIMITATIONS OF THE EXPERIMENT

The results obtained in the experiment give a great approximation of the fetal neck manipulation that is required in fetuses who undergo FETO. The materials and the methodology have a determinant influence in the results of a study. In this case, the objective was to run the experiment in conditions that resemblance as much as possible the real situation. Every decision, in terms of materials, dimensions and experimental setup, was made thoroughly. However, the experiment has some limitations which might have led to some possible errors in the results.

While determining the dimensions of the respiratory tract, the size of the respiratory system of a 27 weeks fetus was considered. However, it was decided to use a tubing of 3 mm for all the respiratory tract but actually just the trachea has that diameter. Moreover, in the respiratory tract that I built just the oropharynx and a little part of the laryngopharynx should be included. I decided to use the total dimension of the pharynx because I considered that the difference was not significant.

It was assumed that during the procedure the neck of the fetus was just in two different positions. I know that in the real surgery that does not happen because there are small variations in the position of the fetal head throughout the procedure. However, I thought that the most important was to determine the total extension that the neck undergoes.

Even though the ultrasound images have a very good quality and the identification of the structures could be made quite easily, the assumptions and considerations taken to determine the location of the centre of rotation of the neck and the position of the lines which defined the angle measured, could have led to some errors. First, the back of the fetus was considered to be horizontal and still during all the procedure. Second, the cervical vertebrae was treated as a unique segment, assuming that all the cervical segments moved together having all of them the same angle respect to the back.

Despite all the weaknesses mentioned above, I strongly think that the results are reliable which confirm that the extension that the neck undergoes in FETO is excessive and it is a real hazard for the baby's wellbeing.

12 CONCLUSIONS

For fetuses with CDH and poor prognosis, the only chance they have to survive after birth is to undergo Fetoscopic Tracheal Occlusion. The outcome of those babies increases considerably after FETO. Even though FETO is an effective procedure that is saving the life of many babies, they are some aspects related to the surgical instrumentation that should be improved so that some complications can be prevented.

The use of rigid fetoscopes requires the hyperextension of the fetal neck. Experimentally ultrasound images which show clearly the position of the fetal head were taken and used to measure the head extension that the fetus undergoes in FETO. The results showed that the neck experiences an extension of 50 degrees throughout the procedure. The neck is significantly hyperextended. Furthermore, that hyperextension is forced by the surgeon during the procedure making use of the fetoscope. These two last facts give evidence that rigid fetoscopes can cause damage to the fetus.

The last problems could be overcome using a flexible fetoscope, which allows the entrance in the trachea without any fetal manipulation.

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15 APPENDICES

15.1 APPENDIX 1

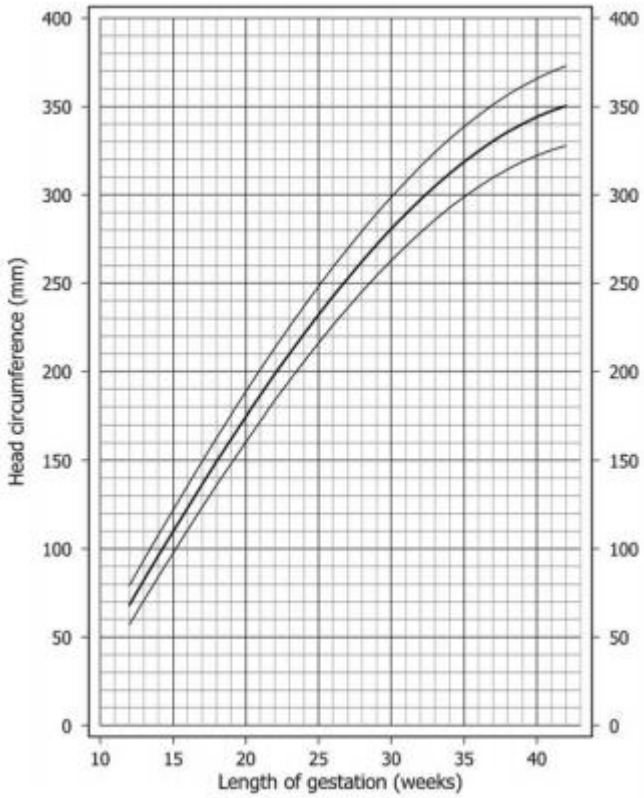


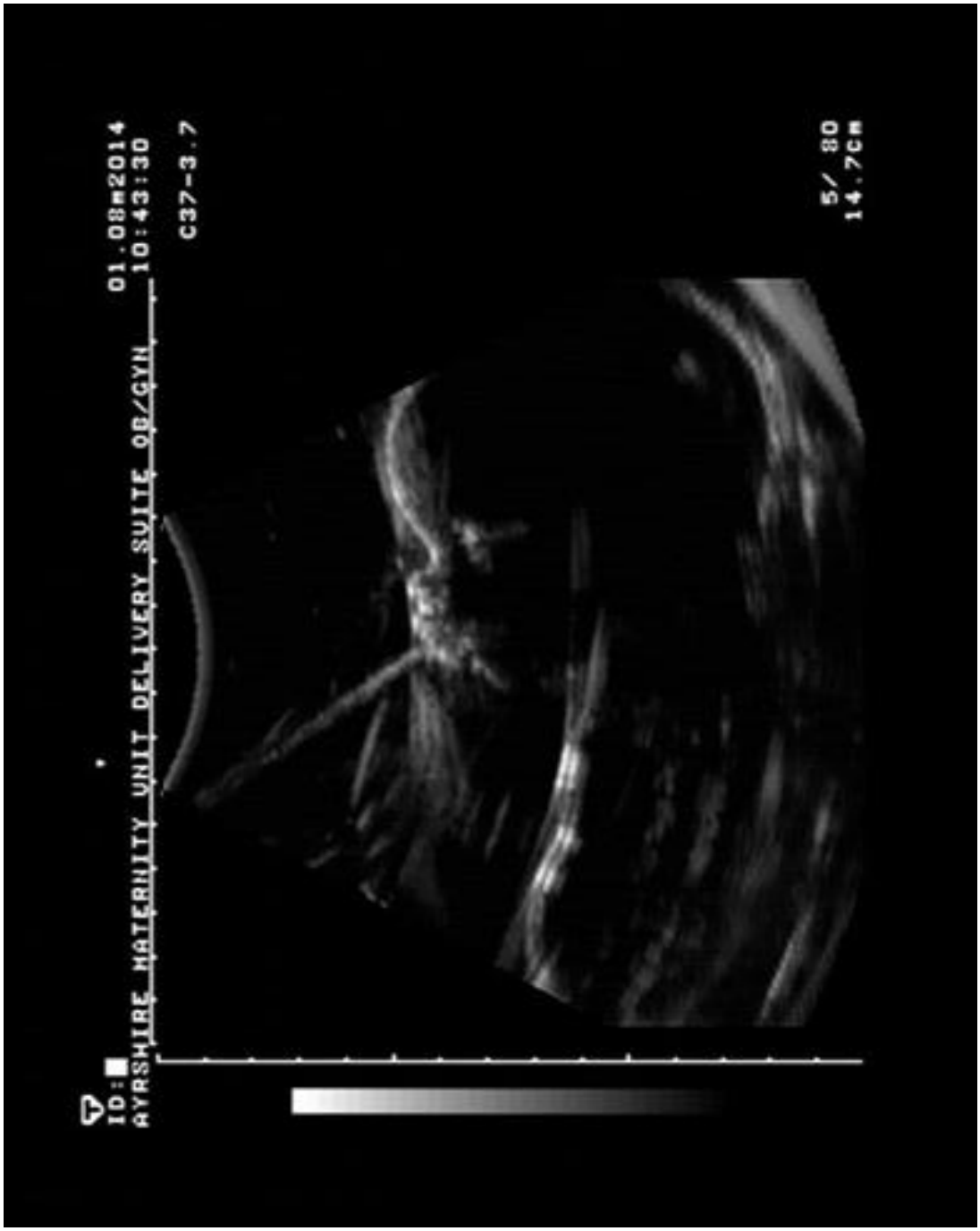
Figure 48. Head circumference size chart[93]

	GA (weeks + days)		
Head circumference (mm)	50th centile	5th centile	95th centile
80	12+4	11+3	13+5
85	12+6	11+6	14+1
90	13+2	12+2	14+4
95	13+5	12+4	15+0
100	14+1	13+0	15+3
105	14+4	13+3	15+5
110	15+0	13+6	16+1
115	15+3	14+2	16+4
120	15+6	14+5	17+0
125	16+2	15+1	17+3
130	16+4	15+4	17+6
135	17+0	15+6	18+2
140	17+3	16+2	18+5
145	17+6	16+5	19+1
150	18+2	17+1	19+3
155	18+5	17+4	19+6
160	19+1	17+6	20+2
165	19+3	18+2	20+5
170	19+6	18+5	21+1
175	20+2	19+1	21+4
180	20+5	19+3	22+0
185	21+1	19+6	22+3
190	21+4	20+2	22+6
195	22+0	20+4	23+2
200	22+2	21+0	23+5
205	22+5	21+3	24+2
210	23+1	21+5	24+5
215	23+4	22+1	25+1
220	24+0	22+4	25+5
225	24+3	22+6	26+1
230	24+6	23+2	26+5
235	25+3	23+5	27+1
240	25+6	24+1	27+5
245	26+2	24+3	28+2
250	26+5	24+6	28+6
255	27+2	25+2	29+3
260	27+5	25+5	30+0
265	28+2	26+1	30+4
270	28+6	26+4	31+2
275	29+3	27+0	32+0
280	30+0	27+3	32+4
285	30+4	27+6	33+3
290	31+1	28+3	34+1
295	31+5	28+6	35+0
300	32+3	29+3	35+6
305	33+1	30+0	36+5
310	33+6	30+3	37+4
315	34+4	31+0	38+4
320	35+3	31+5	39+4

Figure 49. Head circumference calculated from BPD and OFD measurements[93]

15.2 APPENDIX 2

15.2.1 Measurement of head angle in Position 1



15.2.2 Measurement of head angle in Position 2